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Original Communications.

*A PHYSIOLOGICAL AND THERAPEUTIC STUDY OF HYDRASTIS CANADENSIS.**

By David Cerna, M.D., Ph.D.,† Philadelphia, Pa.

FROM *Hydrastis Canadensis*, or golden seal, yellow puccoon, yellow root, orange root, Indian turmeric, or Indian dye, as it is variously and commonly called, a plant belonging to the order of the Ranunculaceæ, are extracted certain active principles, not all of which have yet been fully determined.

The first observer who investigated the chemical composition of this perennial herb was Mr. Alfred A. B. Durand, of this city.‡ It was found by him to contain, besides various other substances, a peculiar nitrogenous crystallizable body, for which he proposed the provisional name of *hydrastine*, suspecting it to be, nevertheless, an alkaloid.

Later it has been ascertained that this new substance is really an alkaloid, known at present as *hydrastine*, having as synonymes *hydrastin* and *hydrastia*, and the honor of

* An essay to which the Prize, for 1890, was awarded by the Medical Society of the County of New York.

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‡ *Amer. Journ. of Pharm.*, 1851, p. 112.

purifying it for the first time belongs to Mr. J. Dyson Perrins, of London.*

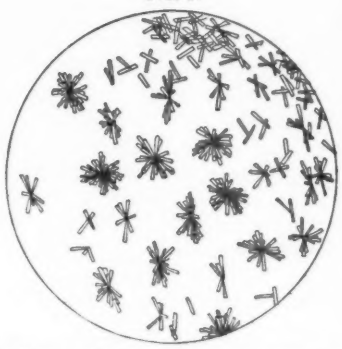
Besides this principle, hydrastis contains, according to Rafinesque,† Kemp,‡ Fleitman,§ Mahla,‖ and Perrins,¶ a second alkaloid, called berberine, found also widely diffused in many other plants; and also a third active principle, volatile in its nature, according to the researches of H. Lerchen,** A. K. Hale,†† of Michigan, and J. C. Burt,‡‡ and generally known in these investigations as "Hale's third alkaloid." Lerchen proposed for this new substance the name of *xanthopuccine*. Recently, however, it is claimed by Professor Power,§§ that *Hydrastis Canadensis* only contains *two* alkaloids,—*hydrastine* and *berberine*.

I will not now enter into the consideration of all the active principles of hydrastis. For the present I shall confine myself to a study especially of *hydrastine*, regarded by most eminent authorities as the principal alkaloidal constituent of this plant.

As stated before, Mr. Perrins was the first investigator to isolate the pure *hydrastine*. More recently it has also been determined, especially by Mr. J. U. Lloyd,‖‖ Professor Power,¶¶ and others. It is generally obtained by exhausting the powder of the rhizome with water by means of percolation, separating the *berberine* as hydrochlorate by the addition of hydrochloric acid to the infusion. The mother liquid is then treated with ammonia in slight excess, and the hydrastine, in an impure state, is precipitated as a brownish powder; but is purified by repeated solutions in boiling alcohol. By this repeated crystallization, with the aid of animal charcoal, the alkaloid is obtained in colorless, or white, shining, four-sided prisms, which become dull when dry.

From the circumstance that hydrastine almost always forms imperfect crystals, it is certainly very difficult to obtain good specimens. With an excellent sample of the pure alkaloid I made several solutions in chloroform, alcohol, and ether, and, after failing several times, I, at last, succeeded in obtaining the crystals from the solution of ether by slow evaporation. An illustration of these crystals is given in Fig. 1.

FIG. 1.



Crystals of the sulphate of hydrastine, seventy diameters.

The white alkaloid of hydrastis, obtained by the method already described, has, according to the analysis of Mahla,*** and later of Professor Power,††† a chemical composition represented by the formula $C_{21}NH_{23}O_6$. Hydrastine is almost insoluble in water, but ether, alcohol, chloroform, and benzine dissolve it easily. It is colored yellowish brown by strong nitric acid, and with sulphuric acid and bichromate of potassium or peroxide of lead it gives a brick-red, assuming after a while a carmine-red color. Mixed with chlorine-water its solution acquires a blue fluorescence. It gives no coloration with concentrated hydrochloric acid, and, according to Professor Power, "concentrated sulphuric acid and monomolybdate of ammonium gives an olive-green color, which appears to be its most characteristic test." The crystals fuse at 135° C. (275° F.), and although generally of an alkaline reaction, they may be said to be tasteless.

Hydrastine can be differentiated from its sister alkaloid *berberine* by the fact that the latter is insoluble in ether, alcohol, chloroform, and benzine. Hydrastine unites with the acids to form salts, which are perfectly soluble in water, with the exception perhaps of the picrate and the tannate.

PHYSIOLOGICAL ACTION OF HYDRASTINE.

General Action.—Comparatively speaking, up to the present time, few investigators have studied the action of this drug upon the lower animals. Among these observers may be men-

* *Lond. Pharmaceut. Journ.*, May, 1862, p. 546.

† "Medical Flora of the United States," 1828, vol. i. p. 253.

‡ *Chemical Gazette*, 1847, p. 209.

§ *Ibid.*, 1847, p. 129.

‖ *Amer. Journ. of Sciences and Arts*, January, 1862.

¶ *Journ. of Chem. Society*, 1863.

** *Amer. Journ. of Pharm.*, 1878, p. 470.

†† *Ibid.*, 1873, p. 248. ‡‡ *Ibid.*, 1875, p. 481.

§§ *Proc. of Amer. Pharm. Assoc.*, 1886, p. 429.

‖‖ *Amer. Pharm. Assoc.*, 1878.

¶¶ *Ibid.*, 1884.

*** *Silliman's Amer. Journ.*, vol. xxxvi., No. 106, 1863, p. 57.

††† *Loc. cit.*

tioned the names of Professor Roberts Bartholow,* Mays,† Fellner,‡ and Slavatinski.§

Bartholow, who appears to have more widely than any of the others extended his general experiments, states that in the frog hydrastine produces muscular rigidity and paralysis of motion, followed by heightened cutaneous reflexes, tonic convulsions from above downward, succeeded by general convulsions with fibrillary trembling between them, and finally tetanus a few minutes before death; that it causes death by asphyxia, as the heart continued to beat after complete cessation of the respiratory movements, and that the cardiac muscular tissue loses its electro-excitability. That in warm-blooded animals (and gives the single example of a rabbit) it produces similar effects, and concludes that hydrastine belongs to the group of the excito-motor agents, heightening perception, cutaneous excitability, and the reflex functions, and causing death by tetanic fixation of the respiratory muscles.

It is regretted, however, that Bartholow's experiments are not detailed, for some of the results obtained in my researches do not entirely agree with his statements, and, besides, I have noticed effects produced by hydrastine not spoken of by him or any of the other writers that I have thus far consulted.

According to Falk,‖ the action of hydrastine is as follows: "In cold-blooded animals, a tetanic stage, with an increase of the reflex activity; a stage of complete paralysis, which commences with paralysis of the motor action of the spinal cord; paralysis of the heart, which first affects the inhibitory ganglia, and then the automatic ganglia; it has a local effect upon musculature. In warm-blooded animals, the paralytic stage begins earlier, and usually precedes the tetanic stage; increased contraction of the vessels, and blood-pressure follows stimulation of the medulla; this is, however, comparatively small, not persistent, but is interrupted by great falls of blood-pressure and vascular relaxation, especially during the tetanic attacks; during the tetanus the lengthening of the pulse takes place through central stimulation of the vagus; the same occurs in the advanced stage of the poisoning; paralysis of the vaso-motor centres follows upon their stimulation; after this, and up to the period of death, there is relaxation of the blood-vessels and fall of blood-pressure. Death, in poisoning by hydrastine, takes place by paralysis of the heart."

In order, therefore, to study more fully the general action of hydrastine, some of the most striking of my experiments are here given in detail. I may state that, for purposes of experimentation, the alkaloid itself, and chiefly its sulphate, have been employed, especially the latter, on account of its solubility.

Experiment 1.—Frog. Injected at 12.45 P.M. .002 gramme; 12.55, animal lies on his back motionless, and respirations are labored; has had convulsions, and shows a marked increase of reflex activity; 1.00, frog is placed on its belly, but is unable to move; is entirely paralyzed; 1.10, tetanic convulsions come on again; 1.20, breathing very much diminished, and heightened reflexes still noticeable; 4.00, paralysis is beginning to disappear, and movements are about normal, as is also the respiratory function; 4.15, frog can leap as when entirely well, and it appears that it will recover. Died next day, about five o'clock in the evening, in convulsions. After death, both muscles and nerves would not respond to faradization.

Experiment 2.—Frog. Gave hypodermically .005 gramme at 1.10 P.M.; 1.15, voluntary movements are slow, but reflex action is increased, as the slightest touch elicits convulsive movements; 1.17, paralysis is complete; 1.20, convulsive movements of tetanic character from above downward; 3.00, respirations have stopped entirely, but heart continues to beat; 3.30, animal is dead, and the heart, which has ceased in diastole, has its cavities distended with black blood. Muscles and nerves respond feebly, but only to powerful faradic current.

Experiment 3.—Frog. At 2.50 P.M. injected subcutaneously .002 gramme; 2.55, animal goes into well-marked tetanic convulsions; 3.00, breathing has stopped, but the heart continues its action; there is a very decided increase in the reflex activity, and the slightest touch of the skin produces powerful general spasm; paralysis has set in; 4.40, heart continues to beat, and convulsions can still be provoked by mechanical irritation. The animal died eventually.

Experiment 4.—Frog. Injected hypodermically at 3.25 P.M., .005 gramme; 3.30, animal quiet; 3.32, convulsive movements

* Lloyd's "Drugs and Medicines," vol. i., 1884–85.

† THERAPEUTIC GAZETTE, 1880.

‡ *Wein. Med. Jahrbücher*, 1885.

§ *Lancet*, May, 1886.

‖ *London Med. Recorder*, April 20, 1890, p. 136; *Virchow's Archiv*, Bd. 119, s. 389.

appear; 3.35, the batrachian is placed on its back; tetanic convulsions manifest themselves, and there are decided evidences of heightened reflexes; 3.46, paralysis is complete; 3.53, respiration has ceased, but the heart continues to act; 4.45, frog is dead. Stimulation by electricity elicited no response in either muscles or nerves.

Six other experiments gave similar results, and from these it may be inferred that hydrastine is a powerful poison to cold-blooded animals, producing in them the following general effects: Muscular rigidity, an increase in reflex activity, tetanic convulsions, paralysis, and finally death by failure of the respiration.

A series of experiments was made to determine the minimum fatal dose of hydrastine in the frog, as is shown in the following examples:

Experiment 11.—Frog; weight, 30 grammes. An injection of .003 gramme is given at 1.45 P.M.; 2.00, animal is convulsed, and shows a condition of increased reflex activity; 2.12, is completely paralyzed; 3.12, continues very feeble and respiration is labored; 6.00, animal still very sick, and finally dies.

To two other frogs of the same weight the same dose was administered with similar untoward effects.

Experiment 14.—Frog; weight, 30 grammes. .001 gramme was given hypodermically at 12 M. The usual symptoms, though feeble in character, were developed, and finally death, in about twenty four hours, followed.

Experiment 15.—Frog; weight, 35 grammes. Received the same dose as last one, and although the animal labored under the influence of the drug for over thirty hours, it finally made a complete recovery.

Experiment 16.—Frog; weight, 32 grammes. The batrachian received hypodermically .001 gramme at 1.40 P.M.; 1.55, animal is perfectly paralyzed, but shows heightened reflexes; 2.15, breathing is labored; 4.55, paralysis begins to disappear; 5.10, animal can move and leap about as in a normal condition. All next day he appeared entirely well. On third day, frog continued apparently in good health, but at 11 A.M. tetanic convulsions returned, with the same increase of reflex activity, and died at 12.30.

From the foregoing observations it is ascertained that the minimum lethal dose of hydrastine in the common frog (*Rana esculenta*) is about .001 gramme for every thirty grammes of the animal's weight.

The effects produced by hydrastine in warm blooded animals resemble those exhibited in cold-blooded animals, but in these other phenomena manifest themselves, as will be seen in the following experiments:

Experiment 17.—Dog; weight, 4 kilos. At 1.55 P.M. gave by jugular vein .020 gramme of the sulphate; 4.10, a slight salivation appears. No other symptoms were noticed, and the animal recovered entirely.

Experiment 18.—Dog; weight, 6 kilos. Injected hypodermically 2 grammes at 12.05 P.M. No effects were produced.

Experiment 19.—Dog; same weight as last. Exposed jugular vein, and injected into it 1 gramme of drug at 11.45 A.M.; 11.46, breathing is arrested, and at 11.47 a violent tetanic convulsion sets in, which ends in death.

Experiment 20.—Mouse. Gave hypodermically .010 milligramme at 10.45; 10.46, respirations are hurried; 10.48, falls to one side, perfectly helpless; 10.50, violent convulsions appear; respirations are exceedingly labored; 10.52, the animal dies.

Experiment 21.—Dog; weight, 3 kilos. Administered subcutaneously .50 gramme at 11 A.M. No effects were produced, with the exception of slight salivation.

Experiment 22.—Pup; weight, 1½ kilos. At 1.45 P.M. received hypodermically .25 gramme; 2.30, no symptoms were observed, and at 2.35 gave .25 gramme more under the skin; 3.10, very pronounced salivation is noticed; 3.20, vomited mucus, and continued to salivate profusely; 4.00, vomited again; 4.10, retches, and once more vomited white, frothy mucus, and some biliary matter; is now quiet. Continues in this condition until six o'clock. Next morning by ten o'clock the animal had completely recovered.

A few days afterwards the same animal succumbed to a dose of .50 gramme after presenting the same symptoms, but in an aggravated form.

Experiment 23.—Pup; weight, 2 kilos. The animal received subcutaneously 1 gramme of drug about 3.30 P.M.; 4.00, is quiet, and licks his lips frequently; 4.15, salivation appears; 4.20, vomited white, frothy mucus; salivation is very profuse; 4.35, very uneasy, with frequent movements of the head to both sides; staggers; 4.40, falls to his side several times, and with difficulty regains his upright position; 4.44, has fallen on his right side, and is now unable to get up; his respirations are very laborious; 4.45, has a tetanic convulsion, which is followed by others of a clonic character; 4.47, convulsions cease a little, and the animal gives a series of shrieking

cries; 4.48, another tetanic convulsion, his head being powerfully thrust backward; 4.50, convulsions again cease, and dog utters cries anew; 5.05, respiration has stopped, but the heart continues to act; 5.07. animal dies in a tetanic convulsion, and immediately becomes stiff. Post-mortem examination showed that the heart had stopped in a diastolic condition, and was non-irritable. No other marked lesion was noticeable in the other organs, with the exception of a slight congestion of the lungs, some peristalsis, and a greenish coloration of duodenum, due, undoubtedly, to biliary extravasation.

Experiment 24.—Pup; weight, 1 kilo. Injected hypodermically .25 gramme of hydrastine at 12.25 P.M.; 12.30, begins to salivate; 12.40, vomits white, frothy mucus, and defecates; 12.50, retches and vomits again; 12.55, the emesis continues; 1.25, animal is very weak, and lies on his side unable to get up; 1.45, has clonic spasms; 1.55, tetanic convulsions appear, and on ceasing, the little pup utters several shrieking cries; 2.20, vomits biliary matter; 3.35, animal is much better, and only vomited now a watery discharge, mixed with bile; is very quiet, but able to stand up; 3.50, has gone to sleep; 3.55, is awakened, and vomits again; 4.00, is sound asleep; 8.30, the little pup has apparently recovered, and runs about. Next morning by ten o'clock the animal has marked stiffness of the jaws, and is exceedingly weak; lies down, with limbs perfectly relaxed. Continued in this condition until about 11 P.M., when he ceased to breathe, the heart continuing to beat for at least fifteen minutes later, when life was extinguished. Post-mortem examination showed no other prominent signs than the ones already mentioned; a slight congestion of lungs, diastolic arrest of the heart, some peristalsis, and a marked biliary extravasation.

Experiment 25.—Rabbit: weight, 2 kilos. Rodent received hypodermically 1 gramme at 10.40. No marked symptoms were produced for about an hour, with the exception of a slight salivation and an apparent increase in the number of respirations; 11.45, muscular tremblings are manifested, with loss of voluntary movements; sensibility somewhat heightened; 12.05 P.M., complete paralysis, followed by convulsions of a tetanic character; loss of sensation, as pinching elicits no pain; 12.45, respirations are gasping in character, and there is intense cyanosis of tongue and ears; heart continues to act forcibly; 1.00, breathing has stopped, but the cardiac viscus is still active; 1.12, animal dead.

Experiment 26.—Pigeon; weight, 2 hectogrammes. Bird received subcutaneously .50 gramme of hydrastine at 11.15 A.M.; 11.35, very uneasy; 12.40, falls to one side, with difficult respiration; 12.45, tetanic convulsions, gasping respirations, and death a few seconds afterwards.

Experiment 27.—Dog; weight, 5 kilos. Injected hypodermically .02 gramme of drug at 1.25 P.M. Rectal temperature before injection was 38° C. 1.45, vomits and salivates profusely; appears uneasy; 1.50, vomits again some biliary matter; 2.25, dog extremely weak; rectal temperature, 37.15° C.; 2.40, has general muscular tremblings; 2.50, tetanic convulsions set in; 3.25, rectal temperature, 37.20° C., and appears much better; 3.40, vomits again, watery discharge mixed with bile; 8.25, animal appears to have recovered, and his temperature has returned to normal,—38° C.

From the evidence brought forward by other observers and from my own general experiments, it is found that hydrastine is, in sufficiently large doses, a poison to both cold- and warm-blooded animals. In the first class of animals it produces a primary increase of the respiratory movements, followed by a decrease and final cessation of the same; muscular tremblings and rigidity; loss of voluntary movement; clonic and tetanic convulsions; increased, at first, and afterwards decreased reflex activity, and, lastly, death by failure of the respiration. It also exhausts the irritability of the muscles and the motor nerves, and very likely exercises an action upon both the sensory nerves and the sensory tract of the spinal cord. The drug likewise destroys the electro-excitability of the cardiac muscle, as that organ, which is always arrested in diastole, does not, after its stoppage, respond to faradization.

In warm-blooded animals, hydrastine produces similar effects: a primary stimulation, a decrease secondarily, and final cessation of the respiratory functions; heightened sensibility followed by a fall below normal; salivation; an increased flow of bile; vomiting; hyperperistalsis; loss of voluntary movement; paralysis; clonic and tetanic convulsions, and finally death by respiratory failure. It also exhausts the excitability of the cardiac muscular fibre, and diminishes bodily temperature.

Post-mortem examinations of the animals killed by hydrastine show, to the naked eye, no marked lesions of the internal organs, with the exception, perhaps, of a slight con-

gestion of the lungs, and a decided biliary extravasation. In order to study the changes which the drug might produce in the intimate constitution of the tissues themselves, these were examined microscopically in two cases, one of comparatively quick and the other of slow poisoning. In the first instance, the animal experimented upon died in four hours; in the second, the dog succumbed within three days.

The histological changes produced in the organs examined are not perhaps very remarkable, but I do not think it will be uninteresting to give a short description of them:

FIRST PUP.—*Brain.*—The organ does not show any changes, except a considerable number of cells, which are likely to be due to the young age of the animal.

Heart.—Normal in every respect.

Liver.—All the blood-vessels are dilated, especially the portal veins, and there is also dilatation of the bile-ducts, which show, besides, catarrhal changes. The liver-cells are slightly cloudy, swollen, and exhibit a more granular protoplasm than normally, the nuclei being less distinct.

Lung.—There is decided congestion of both pulmonary arteries and veins, and have in many places small thrombi. The blood-vessels are enormously dilated. The air-vesicles are overdistended, stretched out, presenting the character of an emphysematous lung. The alveolar septa between the elements are all thickened, and the connective tissue, doubtless through an irritative action, shows a cellular infiltration. The cell proliferation is quite prominent around the blood-vessels and the smaller bronchi. The epithelial lining of the air-vesicles and the bronchi is distinctly swollen and irritated.

SECOND PUP.—*Brain.*—Normal.

Heart.—In general the muscular tissue appears anæmic, most of the capillaries being empty. The muscular fibres show slight fatty metamorphosis. The cavities are filled with coagulated blood, and within these blood-masses large crystalline bodies of a dark-brown color are found, the crystals being somewhat needle-shaped and arranged in large bundles. Possibly they are hæmatoidin crystals.

Liver.—The hepatic cells are slightly atrophied, and the most of them infiltrated with fat, which appears in minute and large droplets. Some of the cells are completely converted into fat-vesicles, and are highly transparent, yet they have a sharp, definite contour, and retain admirably their pentagonal shape. The connective tissue does not seem to be increased, and both blood-vessels and biliary ducts are apparently normal. Some of the veins, especially the portal, contain blood; while the hepatic arteries and veins are empty. On the whole, the liver tissue may be considered as anæmic.

Lung.—The air-vesicles are distended, and some of them seem to have lost their alveolar septa, and to have stretched out into a common cavity, such as is found in emphysematous conditions. This is particularly marked near the edges of the lung. The bronchi are also dilated, and contain in their luminæan inflammatory (catarrhal) exudate, composed of desquamated epithelium, leucocytes, red blood-corpuscles, and mucus. The walls of the air-vesicles are, in most instances, intact, though evidently thickened. This thickening may be ascribed chiefly to an increase of the luminæ of the pulmonary capillary blood-vessels, due to overdistended blood-corpuscles, partly to the thickening of the septa referred to, and also to an infiltration of leucocytes. The air-vesicles are empty, although in a few instances some disintegrated material may be seen within the luminæ, having its source in an inflammatory exudate.

Kidney.—The epithelium is cloudy and swollen, so that the luminæ of the tubules are accidentally obstructed. This condition can best be seen in transverse sections; the blood-vessels may be considered anæmic; their walls, the connective tissue, and the Malpighian tufts appear to be normal.

From my own experiments, it is also determined that the minimum fatal dose of the drug in the dog, by hypodermic injection, is .50 gramme for every kilogramme of the body-weight.

Another interesting property is attributed to hydrastine, but which I have had no opportunity, so far, to corroborate. Fellner and A. T. Slavatinski* affirm that the alkaloid has a distinct and powerful ecbolic action. The latter experimenter found that in doses of from .01 to .03 gramme per kilogramme of the body-weight, hydrastine produces contraction in the fibres of the non-pregnant uterus.

A better knowledge of the physiological action of hydrastine can be obtained from studying the behavior of the drug on the different systems separately. I shall then proceed to make such a study.

* London *Lancet*, May 22, 1886.

ACTION ON THE MUSCULAR SYSTEM.

Hydrastine, in small doses, appears to have a stimulating effect on the muscular tissue. Toxic quantities, however, as may have been observed, destroy the excitability of the muscles in general, and especially of the cardiac muscular fibre, as both structures fail under such circumstances to respond to faradization. The following experiments illustrate this:

Experiment 28.—Frog. Destroyed brain and exposed calf-muscles. The shock having passed off, an injection of hydrastine was made into abdominal cavity at 11.25 A.M.; 11.45, muscular rigidity appears, followed soon after by tetanic convulsions. A faradic current is applied to exposed muscles, and these respond but feebly; 12.15, complete paralysis; respiration exceedingly labored; the same current is again applied to the muscles, but no contractions are produced.

Experiment 29.—Frog. Had his brain destroyed, and tied artery of the left posterior limb; exposed muscles of both calves. When the animal had recovered from the shock, he received hypodermically a lethal dose of the drug at 3.10 P.M.; 3.25, muscular tremblings and spasm are present; respiration difficult; 3.30, tetanic convulsions are observed; faradization of muscles of poisoned limb produces feeble contractions; muscles of left limb respond readily to the same current; 4.15, breathing has ceased, but heart continues to act. Electrical stimulation of the muscles of left limb elicited the usual contractions; no such effect could be observed in the muscles of poisoned leg.

Experiment 30.—Placed a cut-out heart of a frog in a solution of hydrastine. After the viscus has ceased to act, faradization was applied, but no response was elicited.

These experiments were repeated, with similar results. Experiments made with Marey's myograph show clearly the depressant action of hydrastine on the irritability of muscle. Usually the gastrocnemius of a frog was carefully prepared, connected with the instrument and with a common Dubois-Reymond's electrical apparatus and the corresponding key, in order to apply both the opening and closing shocks.

There appears to be at first, especially under minute doses, a period of excitement or stimulation, for in such a period the height of the curve is greater than normal, and the contraction somewhat prolonged. Gradually, however, the muscular irritability is diminished, and continues thus until it is entirely abolished. Under large doses there is no period of excitement.

This lessened excitability of the muscular fibre is not due, as might be supposed, to an exhaustion produced by the frequent application of electrical stimulation, but to the action of the drug, as shown by the results obtained in the normal and poisoned muscle, in the same period of time and subject both to the same currents. This has already been proven in previous experiments.

I will detail in the following tables some of the experiments performed:

TABLE AH.—*Experiment* 57.—Animal, frog; weight, 25 grammes.

Time. h. m.	Height of contraction in mm.	Remarks.
.....	...	Gastrocnemius of frog prepared. Stimulation at 15 c.c. between coils.
10.10	28	
10.12	...	Hypodermic injection of .001 gramme.
10.27	32	
10.32	20	
10.37	16	
10.40	...	Tetanic convulsions.
10.42	16	
10.47	16	
10.52	16	
10.57	10	
11.03	6	

TABLE CH.—*Experiment* 59.—Animal, frog; weight, 24 grammes.

Time. h. m.	Height of contraction in mm.	Remarks.
.....	...	Gastrocnemius prepared. Stimulation at 13 c.c. between coils.
12.08	30	
12.14	30	
12.30	28	Injection of .005 gramme.
12.35	16	
12.39	16	
12.48	16	
1.05	12	
1.32	6	
1.34	4	

ACTION ON THE NERVOUS SYSTEM.

Hydrastine, resembling strychnine in its action, produces an increased condition of the reflexes; clonic, but more frequently tetanic, convulsions and paralysis.

Reflex Action.—That the alkaloid produces a primary hyperexcitability of the reflexes is proven by the following experiment:

Experiment 31.—Frog. Brain destroyed, and waited for the shock to pass away. A beaker of water slightly acidulated with sul-

phuric acid was prepared; in it the right flaccid leg of the batrachian was immersed. Reflex action took place in eight seconds at 11.35 A.M. At 11.37 an injection was made into the abdominal cavity; 11.48, reflex action in two seconds; 11.50, reflex action in two seconds; 11.55, reflex action in three seconds; convulsions appear; 12.15, reflex action in five seconds; animal is paralyzed; 12.30, reflex action in eight seconds; 1.15, reflex action in twelve seconds; 1.30, reflex action in twenty seconds. The decrease of the reflexes continues gradually up to death.

This primary stage of increased reflex activity takes place when the iliac artery or the abdominal aorta has been tied before the administration of the drug. The examples that follow sufficiently explain themselves:

Experiment 32.—Frog. After the cerebrum was destroyed, the right sciatic nerve was dissected and isolated; then a tight ligature was applied around all the tissues, except the nerve, and waited for the shock to pass off. At 2.15 P.M. reflex action was observed in twelve seconds; 2.20, a subcutaneous injection of hydrastine was made into the anterior part of the frog's body; 2.40, protected limb was immersed in the acidulated solution, and reflex action was manifested in three seconds; 2.45, immersion of poisoned limb, reflex action in three seconds; 2.48, immersion of ligatured limb, reflex action in three seconds; 2.50, paralysis has ensued, as the animal will lie in any position in which it is placed; 2.58, immersion of unprotected leg, reflex action in six seconds; 2.59, immersion of non-poisoned limb, reflex action in four seconds; 3.02, powerful tetanic convulsions; 3.20, immersion of either foot, reflex action in fifteen seconds; 3.45, reflex action in twenty seconds. This depression is now steady, until it appears to be abolished just before death.

Experiment 33.—Frog. Tied abdominal aorta after ablating cerebrum, and, the shock having passed, reflex action in lower extremities was observed in ten seconds. At 3.15 an injection of the alkaloid was made in anterior part of the body; 3.25, reflex action in two seconds; 3.40, reflex action in two seconds; 3.45, reflex action almost immediately, and powerful convulsions are induced; 3.50, reflex action in three seconds; 3.55, reflex action in three seconds; 4.00, reflex action in four seconds; 4.15, reflex action in six seconds, and convulsions again; 4.45, reflex action in twenty-two seconds; 4.55, reflex action in thirty seconds.

The fact, then, that increased reflex activity is produced by hydrastine, after tying the peripheral arteries, shows that such an increase is of central origin, and is not due to any peripheral influence.

From a close observation of the preceding experiments another important fact is gleaned: that motion is lost before sensation, a fact that is directly opposite to the assertion of Mays's,* that sensation is lost before motion.

To explain the depression and the final abolition that follow the primary stage of increased reflex activity, I am led to take two important factors into consideration,—the sensory nerves and Setschenow's inhibitory centre in the medulla oblongata.

In corroboration of Mays's experiments, I have found that hydrastine produces anæsthesia when locally applied to the nerves; that, however, the depression of reflex activity in the poisoned frog is not due to a depression of the sensory nerves is shown by the fact, which I have observed, that high section of the cord induces a return almost to normal of the reflexes. This appears to show that the drug exercises a stimulant action on the chief inhibitory centre that controls reflex action. The details of one experiment will illustrate this point.

Experiment 34.—Frog. After the shock, from the operation to destroy cerebrum, had passed, reflex action was induced in five seconds. At 11.10 A.M. the frog received a subcutaneous injection of hydrastine; 11.35, reflex action in two seconds; 11.50, reflex action in four seconds, convulsions set in; 12.10, reflex action in four seconds, convulsions continue; 12.45, reflex action in thirty seconds; 12.48, severed cord in lower cervical region; 1.15, reflex action in twenty seconds; 1.40, reflex action in twelve seconds, animal paralyzed; 2.15, reflex action in thirty-five seconds; 2.40, reflex action in one minute and ten seconds; 3 00, no reflex action in five minutes.

For the present, therefore, I must come to the conclusion that hydrastine later in the poisoning diminishes, and finally abolishes, reflex activity through a double action,—that is, by stimulating, at first, Setschenow's centre in the medulla oblongata, and afterwards by paralyzing the spinal cord.

Motor Nerves.—It has been stated that, after death in the frog, through the action of hydrastine, faradization of the sciatics failed to produce contractions of the tributary mus-

* *Loc. cit.*

cles; and even this has been observed to be the case when these muscles could be induced to respond to the same current directly applied to them, showing that the motor nerve-trunks are overpowered by the alkaloid. The following experiments and examples of many others clearly show this action of the drug:

Experiment 35.—Frog. Prepared in the usual way, and exposed both sciatics. A ligature was placed around the left leg, excluding the corresponding nerve. An injection was made into the abdominal cavity at 2.35 P.M. The usual symptoms of poisoning by the alkaloid followed soon afterwards; 2.45, faradization of nerve of protected limb produced contractions of gastrocnemius; the muscles also responded readily to the same current; on stimulation of poisoned sciatic, feeble contractions of tributary muscles are induced; 3.10, no contractions of corresponding muscles are produced by faradization of the right sciatic; to the same current, applied to the nerve of ligatured leg, the respective muscles respond still, although not so readily. After death both nerves failed to act on electrical stimulation.

Experiment 36.—Frog. Ablated cerebrum and exposed both sciatics. On left nerve was placed locally a strong solution of hydrastine; on right sciatic, a weak salt solution, to prevent action of surrounding atmosphere. After a certain length of time (a little over two hours), faradization of right sciatic showed, of course, that this nerve was intact, but the same stimulus applied to poisoned sciatic failed to produce contractions of tributary muscles.

Hydrastine, therefore, paralyzes or exhausts the irritability of the motor nerves.

Paralysis.—My experiments show that the alkaloid under consideration destroys or depresses functional activity of the spinal cord, of the motor nerve-trunks, and of the muscles. So that it would appear that the paralysis which it causes is due to a depression of the whole motor apparatus.

Convulsions.—One of the most characteristic effects of hydrastine on the lower animals, especially the frog, is the production of convulsions, which are more commonly of a tetanic nature. These are observed all over the body, even when the abdominal aorta is ligated previous to the administration of the drug, thus cutting off the action of the alkaloid upon the parts deprived of the blood-supply. This is shown in Experiment 33, and from such a result it is inferred that the convulsions are not peripheral. That they are not cerebral is proven by the fact that they still occur after section of the cord.

Experiment 38.—Dog; weight, 3 kilos. Cut cord in cervical region. At 2.15 P.M. administered hypodermically 2 grammes of the drug; 3.30, has general tetanic convulsions, which continue at short intervals; 5.45, animal dies in a powerful tetanic convulsion.

Experiment 39.—Frog. After the animal was pithed, the spinal cord was exposed and destroyed as carefully as possible. This done, the batrachian received into abdominal cavity a dose of the alkaloid at 3.20 P.M. Animal dies at 6.15, but no convulsive movements of any kind occurred.

The convulsions produced by hydrastine, therefore, are of spinal origin.

ACTION UPON THE CIRCULATION.

Fellner,* Slavatinski,† and Bartholow‡ have, to a certain extent, studied the action of hydrastine upon the circulation.

Slavatinski affirms that the drug, in medium doses, paralyzes the vaso-motor centres, and thus decreases blood-pressure; that it acts on the heart first as a stimulant, and afterwards as a depressant of the motor ganglia, and that no effect seems to be produced on the peripheral endings of the pneumogastrics.

By Fellner it is asserted that large doses produce a transient rise in the arterial pressure, followed by a depression of the same; that medium-sized doses produced the same phenomena, only in a less prominent degree; that small quantities are followed by a slight diminution of the blood-pressure, succeeded very soon by a permanent rise; that division of the splanchnics or compression of the abdominal aorta did not materially change the above-described effects; that division of the spinal cord was not followed by any rise of the arterial pressure; and that, finally, when large doses exercise their depressing action on pressure, strychnine and dyspnœa are capable of elevating this.

Bartholow states that hydrastine acts upon both the inhibitory and motor apparatus of the heart, and that the drug produces a reduction of the blood-pressure.

The results of my own experiments are at variance, in one way or another, with all these investigations, regarding the action of the alkaloid upon the circulation, as will be seen in the course of this paper.

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* *Centralblatt für die Medicinische Wissenschaften*, November, 1884, p. 417.

† *Loc. cit.*

‡ *Loc. cit.*

With regard to the effects produced on the arterial pressure, I agree with Professor Bartholow, notwithstanding the fact that this investigator experimented on chloralized animals, from which no very accurate results can be obtained.

On the Heart.—Hydrastine is undoubtedly a heart-poison. It has been sufficiently proven by previous experiments that the drug, locally applied, or when administered through the circulation, affects directly the cardiac muscle and totally destroys its electro-excitability; but hydrastine appears to exercise no primary influence on the pneumogastrics, as will be seen hereafter.

On the Pulse.—Hydrastine, in small doses, increases the frequency of the heart's action, as will be observed in the following experiment:

TABLE I.—*Experiment* 40.—Animal, dog; weight, 22 kilos.

Time. h. m. s.	Dose.	Pulse in 20 sec.	Remarks.
4.15.00	.....	...	
4.15.20	.....	40	
4.15.40	.....	40	
4.16.00	.010 gramme.	40	Injection into jugular vein begun.
4.16.20	.....	70	Injection into jugular vein ended.
4.16.40	.....	75	
4.17.00	.....	70	
4.17.20	.....	64	
4.17.40	.....	60	
4.18.00	.....	60	

The increase is noticed when the pressure is far below normal, and as the drug does not appear to influence the vagi, it may be inferred that such a frequency depends on a direct primary action upon the intracardiac motor ganglia.

However, the most constant action of hydrastine, in moderate and in large doses, is to diminish the number of the heart pulsations, and at the same time to increase the size of the pulse-waves. The following experiments explain themselves:

Experiment 41.—Frog. Animal was pithed and heart exposed, which was beating 56 times a minute. At 12.02 P.M. injected subcutaneously .002 gramme of the drug; 12.07, heart beats only 26 per minute; 12.09, beats 15 per minute, and the batrachian goes into powerful tetanic convulsions; 12.15, heart beats about 4 times in the minute; the convulsions continue; 12.30, breathing has stopped, spasms continue, and the heart beats about once or twice in the minute.

Experiment 42.—Frog. Exposed heart after cerebrum had been ablated. The cardiac viscus was then beating at the rate of 44 per minute. Injected hypodermically .001 gramme at 11.42 A.M.; 11.45, heart's action slow but strong; beats 20 times in the minute; 11.48, 12 per minute; convulsions set in and respiration stops; 11.50, 8 per minute; and by 12 M. only 5 beats could be counted in the minute.

The same results are noticed when the isolated heart of the frog is placed in a solution of hydrastine.

TABLE II.—*Experiment* 43.—Animal, dog; weight, 5 kilos.

Time. h. m. s. P.M.	Dose.	Pulse per min.	Remarks.
2.00.00	.....	212	Normal animal; right carotid connected with manometer.
2.00.15	.....	200	
2.00.30	.....	200	
2.00.40	.12 gramme.	200	Injection into femoral vein begun.
2.00.55	.....	188	Injection into femoral vein ended.
2.01.10	.....	160	
2.01.25	.....	.....	
2.01.40	.....	132	
2.01.55	.....	76	
2.02.05	.....	.....	Animal dead.

TABLE V.—*Experiment* 46.—Animal, dog; weight, 7 kilos.

Time. h. m. s.	Dose.	Pulse per min.	Remarks.
.....	.....	.....	Normal animal; left carotid connected with kymograph; injection into external jugular vein.
3.15.00	.....	.....	
3.15.20	.....	210	
3.15.40	.....	210	
3.16.00	.....	210	
3.16.20	.10 gramme.	216	Injection begun.
3.16.40	.....	159	Injection ended.
3.17.00	.....	180	
3.17.20	.....	171	
3.17.40	.....	168	
3.18.00	.....	180	
3.18.20	.....	180	
3.18.40	.....	180	
3.19.00	.....	171	
3.19.20	.....	165	
3.19.40	.....	162	
3.20.00	.....	166	
3.20.20	.....	159	
3.20.40	.....	156	
3.21.00	.....	153	
3.21.20	.....	153	
3.21.40	.....	150	
3.22.00	.....	156	

Time. h. m. s.	Dose.	Pulse per min.	Remarks.
3.22.20	.....	150	
3.22.40	.....	150	
3.23.00	.....	150	
3.23.20	.....	150	
3.24.00	.....	153	
3.24 20	.....	153	
3.24.40	.....	150	
3.25.00	.....	147	
3.25.20	.....	150	
3.25.40	.....	147	
3.26.00	.....	144	
3.26.20	.....	144	Killed eventually with chloroform.

The phenomenon of pulse-rate diminution may and does generally depend upon these causes: Stimulation of the cardio inhibitory apparatus, depression of the intracardiac ganglia, changes of blood-pressure, and a direct action on the heart muscle itself.

Now, this depression of the heart's action produced by hydrastine persists after previous section of the pneumogastrics, and even after complete division of the medulla spinalis, as is shown in the experiments detailed below:

TABLE VII.—*Experiment* 48.—Animal, dog; weight, 14½ kilos.

Time. h. m. s.	Dose.	Pulse per min.	Remarks.
11.00.00	.....	.....	Left carotid used; vagi prepared.
11.00.20	.....	264	
11.00.40	.20 gramme.	264	Injection into external jugular.
11.01.00	.....	225	Tetanic convulsions.
11.01.20	.....	171	Injection ended.
11.01.40	.....	171	
11.02.00	.....	180	
11.02.20	.....	180	
11.02.40	.....	195	
11.03.00	.....	195	
11.03.20	.....	192	
11.03 40	.....	156	
11.04.00	.....	168	
11.04.05	.....	.....	Cut both pneumogastrics.
11.04.20	.....	204	
11.04 40	.....	216	
11.05.00	.....	216	
11.05.20	.....	216	
11.05.40	.....	210	
11.06.00	.....	204	
11.06.20	.....	208	

TABLE VIII.—*Experiment* 49.—Animal, dog; weight, 4½ kilos.

Time. h. m. s.	Dose.	Pulse per min.	Remarks.
3.30.00	.....	.....	Right carotid used.
3.30.20	.....	180	Both vagi cut.
3.30.30	.....	192	
3.30.40	.....	264	
3.30.50	.....	270	
3.31 00	.....	258	
3.31.10	.....	258	
3.31.15	.20 gramme.	.....	Injection into external jugular begun.
3.31.20	.....	216	Injection into external jugular ended.
3.31.30	.....	216	
3.31.40	.....	156	
3.31.50	.....	156	
3.32.00	.....	156	
3.32.10	.....	138	
3.32.20	.....	144	
3.32.30	.....	138	
3.32.40	.....	150	
3.32.50	.....	144	
3.33.00	.....	144	
3.33.10	.....	144	
3.33.18	.....	.....	Animal dead.

TABLE X.—*Experiment* 52.—Animal, dog; weight, 15 kilos.

Time. h. m. s.	Dose.	Pulse per min.	Remarks.
.....	.....	.....	Cord cut at lower cervical region; vagi divided; artificial respiration.
4.20.00	.....	156	
4 20.15	.015 gramme.	156	Injected into external jugular.
4.20.35	.....	141	
4.20.55	.....	150	
4.21.15	.....	141	
4.21.35	.....	141	
4.21.55	.....	138	
4.22.15	.....	135	
4.22 35	.....	135	
4.22.55	.....	126	
4 23.15	.....	123	
4.23 35	.....	126	
4.23.55	.....	132	
4.24.15	.....	147	
4.24.35	.....	156	
4.24.55	.....	156	

The alkaloid under consideration does not seem to exercise any influence on the trunks of the vagi, as their section in the poisoned animal (see Experiment 48) produced (although not even to the original rate) an increase in the number of heart pulsations. Again, faradization of the pneumogastrics in the hydrastinized dog causes an instantaneous arrest of the heart.

To judge, therefore, from the results of the foregoing experiments, it appears that hydrastine diminishes the number and increases the volume of the cardiac beats by an action upon the heart-muscle and the intracardiac ganglia.

On the Blood-Pressure.—As stated before, one investigator, Fellner, affirms that hydrastine, under many circumstances, produces a

distinct rise of the arterial pressure, a statement which I have never been able to corroborate.

The alkaloid in minute, medium, and poisonous doses, and whether it is administered hypodermically into the peritoneal cavity or through the circulation directly, invariably causes the column of mercury in the manometer to fall below the normal height. Lethal doses are followed by a fall, which continues up to death, while in small and moderate quantities the decreased pressure gradually rises again, but never above the normal point. This is shown in the following experiments (see also Figs. 2 and 3):

TABLE XI.—*Experiment* 43.—Animal, dog; weight, 5 kilos.

Time. h. m. s.	Dose.	Blood-pressure. mm.	Remarks.
2.00.00	.....	106–122	Normal animal; right carotid connected with manometer.
2.00.15	.....	106–122	
2.00.30	.....	106–122	
2.00.40	.12 gramme.	106–122	Injection into femoral vein begun.
2.00.55	.....	70–80	Injection ended.
2.01.10	.....	70–80	
2.01.25	.....	106–114	
2.01.40	.....	20	
2.02.05	.....	.....	Animal dead.

TABLE XIV. — *Experiment* 46. — Animal dog; weight, 7 kilos.

Time. h. m. s.	Dose.	Blood-pressure. mm.	Remarks.
.....	.....	.....	Normal animal; left carotid connected with kymograph.
3.15.00	.....	118–124	
3.15.20	.....	118–124	
3.15.40	.....	116–128	
3.16.00	.....	110–128	
3.16.20	.10 gramme.	112–132	Injection into external jugular begun.
3.16.40	.....	80	Injection into external jugular ended.
3.17.00	.....	22–30	
3.17.20	.....	24	
3.17.40	.....	22	
3.18.00	.....	14–24	
3.18.20	.....	12–20	
3.18.40	.....	14–22	
3.19.00	.....	14–22	
3.19.20	.....	16–24	
3.19.40	.....	22	
3.20.00	.....	20–26	
3.20.20	.....	22–26	
3.20.40	.....	24–30	
3.21.00	.....	26–32	
3.21.20	.....	30–34	
3.21.40	.....	30–36	
3.22.00	.....	34–40	
3.22.20	.....	36–42	
3.22.40	.....	40–42	
3.23.00	.....	42–50	
3.23.20	.....	46–52	
3.23.40	.....	50–56	
3.24.00	.....	54–60	
3.24.20	.....	56–60	
3.24.40	.....	54–60	
3.25.00	.....	58–64	
3.25.20	.....	60–66	
3.25.40	.....	62–68	
3.26.00	.....	64–72	
3.26.20	.....	64–68	
3.26.40	.....	68–74	
3.27.00	.....	68–74	
3.27.20	.....	76–82	
3.27.40	.....	76–82	
3.28.00	.....	74–78	
3.28.20	.....	74–78	
3.28.40	....	78–82	Killed eventually with chloroform.

TABLE XVI. — *Experiment* 47.—Animal, dog; weight, 22 kilos.

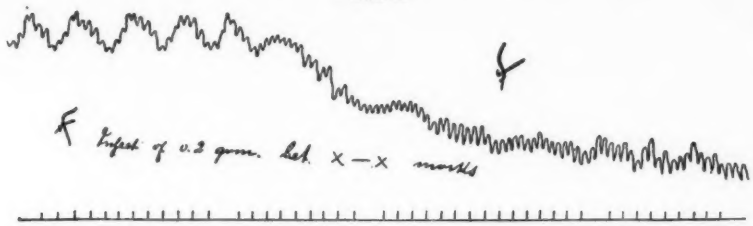
Time. h. m. s.	Dose.	Blood-pressure. mm.	Remarks.
4.15.00	.....	124–144	Normal animal.
4.15.30	.....	124–144	
4.16.00	.010 gramme.	124–144	Injection into jugular vein begun.
4.16.20	.....	90–106	Injection into jugular vein ended.
4.16.40	.....	60–80	
4.17.00	.....	60–80	
4.17.20	.....	64–90	
4.17.40	.....	66–94	
4.18.00	.....	60–102	Struggles.

A depression of the heart's action, due either to a direct cardiac or to an inhibitory influence, and a paralysis of the vaso-motor system, will cause a reduction of the blood-pressure. It is found that the pressure is lowered under hydrastine, after previous section of the pneumogastrics, as will be observed in the experiment detailed below, an example of many others performed.

TABLE XVII.—*Experiment* 49.—Animal, dog; weight, 4 kilos.

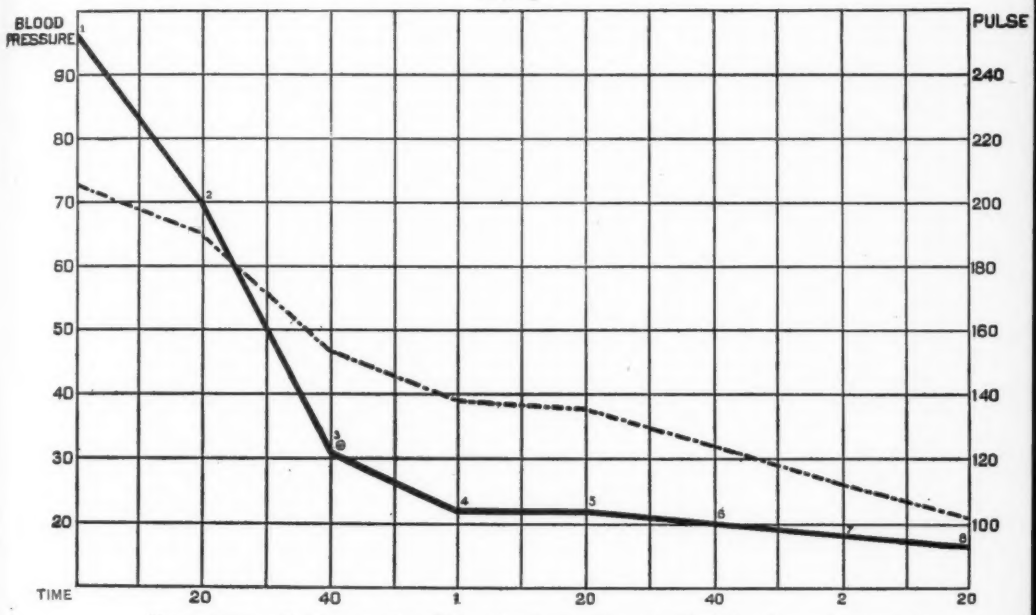
Time. h. m. s.	Dose.	Blood-pressure. mm.	Remarks.
3.30.00	.....	90–124	Left carotid connected with manometer.
3.30.20	.....	110	Cut both vagi.
3.30.30	.....	110–154	
3.30.40	.....	104–118	
3.30.50	.....	90–140	
3.31.00	.....	100–124	

FIG. 2.



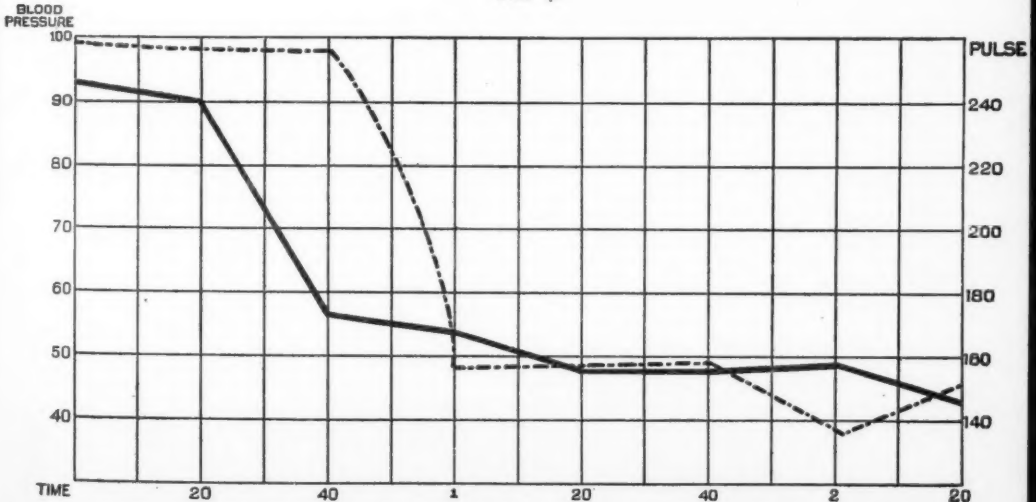
Tracing showing the action of hydrastine on the blood-pressure and the rate and volume of the pulse.

FIG. 3.



HYDRASTINE.—Plot from tracing of Experiment 47. Normal. Black line (———), pressure; broken line (- - - -), pulse.

FIG. 4.



HYDRASTINE.—Plot from tracing of Experiment 49. Vagi cut. Black line (———), pressure; broken line (- - - -), pulse.

Time. h. m. s.	Dose.	Blood-pressure. mm.	Remarks.
3.31.10	.....	80–106	
3.31.15	.20 gramme.	.....	Injection into external jugular begun.
3.31.20	.....	84–96	Injection into external jugular ended.
3.31.30	.....	56	
3.31.40	.....	54	
3.31.50	.....	40–56	
3.32.00	.....	44–56	
3.32.10	.....	44–56	
3.32.20	.....	42–56	
3.32.30	.....	36–50	
3.32.40	.....	36–46	
3.33.18	.....	.....	Animal dead.

The cause, then, of the lowering of the blood-pressure, produced by the drug, resides in the heart itself or in the vaso-motor system. Of several experiments made by severing the cord to produce the corresponding vaso-motor paralysis, before the ingestion of the alkaloid, I only detail two,—one, in which the cord was only partially divided; and another, in which post-mortem examination showed complete section of the medulla spinalis. In both instances, as will be seen, the administration of hydrastine was followed by the usual phenomenon of blood-pressure reduction.

TABLE XVIII.—*Experiment* 51.—Animal, dog; weight, 3 kilos.

Time. h. m. s.	Dose.	Blood-pressure. mm.	Remarks.
.....	.....	.....	Vagi divided; cord partially cut.
3.45.00	.....	140–160	
3.46.00	.....	150–164	
3.46.30	.10 gramme.	150–164	Injection into external jugular begun.
3.46.50	.....	90–100	Injection into external jugular ended.
3.47.10	.....	50	
3.47.30	.....	46	
3.47.50	.....	46	
3.48.10	.....	46	
3.48.30	.....	46	
3.48.50	.....	48	
3.49.10	.....	48	
3.49.30	.....	54	
3.49.50	.....	56	
3.50.10	.....	58	
3.50.30	.....	60	
3.50.50	.....	64	
3.51.10	.....	64	
3.51.30	.....	64	
3.51.50	.....	66	
3.52 10	.....	66	
3.52.30	.....	66	
3.52.50	.....	66	

TABLE XIX. — *Experiment* 52. — Animal, dog; weight, 15 kilos.

Time. h. m. s.	Dose.	Blood-pressure. mm.	Remarks.
.....	.....	.....	Cord cut at lower cervical region;* vagi divided; artificial respiration.
4.20.00	.....	150	
4.20.15	.015 gramme.	150	Injection into external jugular begun.
4.20.35	.....	120	Injection into external jugular ended.
4.20.55	.....	40–60	
4.21.15	.....	30–46	
4.21.35	.....	22–34	
4.21.55	.....	20	
4.22.15	.....	20	
4.22.35	.....	20	
4.22.55	.....	22–30	
4.23.15	.....	22–30	
4.23.35	.....	28–36	
4.23.55	.....	30	
4.24.15	.....	36	
4.24.35	.....	36	
4.24.55	.....	36	
4.25.15	.....	34	
4.25.35	.....	34	

The most obvious conclusion to be drawn from the results of these latter experiments would appear to be that hydrastine diminishes the pressure of the blood by a direct action upon the heart. Such, however, is not the case, and there is sufficient evidence to prove that the drug likewise influences the vaso-motor system.

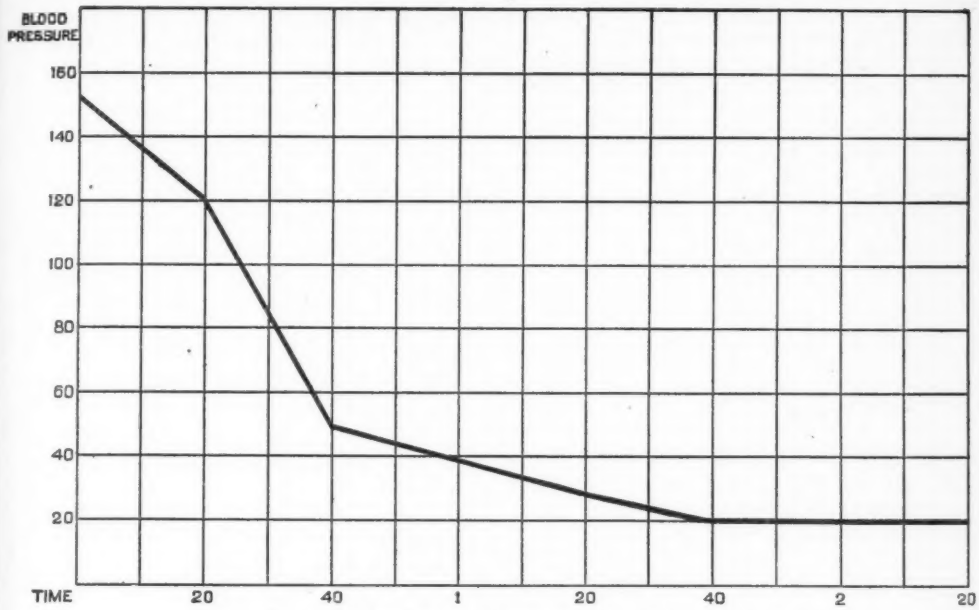
In the normal animal we have generally a lowered pressure taking place *pari passu*, with a diminution in the number of heart-beats, from which we could infer that the phenomenon under consideration was due to a cardiac action. But it is found that in such circumstances neither asphyxia nor faradization of a sensitive nerve (which in the non-poisoned animal would cause a rise in the blood-current) is able to produce appreciable changes in the lowered condition of the arterial pressure, and, if any are noticed, they are those which would be observed in an animal subjected alone to the action of the poison.

The following examples sufficiently explain themselves:

TABLE XX. — *Experiment* 53. — Animal, dog; weight, 9 kilos.

* Verified by post-mortem.

FIG. 5.



HYDRASTINE.—Plot from tracing of Experiment 52. Cord and vagi cut.

Time. h. m. s.	Dose.	Blood-pressure. mm.	Remarks.
3.25.00	.....	112	Normal animal.
3.25.10	.010 gramme.	112	Injection into jugular begun.
3.25.20	.....	100	Injection into jugular ended.
3.25.30	.....	110	
3.25.40	.....	130	Convulsions set in.
3.25.50	.....	114	Convulsions cease.
3.26.00	.....	96	
3.26.10	.....	98	
3.26.20	.....	100	
3.26.40	.....	98	
3.27.00	.....	98	
3.27.20	.....	110	Convulsions.
3.27.40	.....	100	Convulsions cease.
3.28.00	.....	98	Stopped drum five minutes.
3.33.00	.. ..	98	
3.33.20	.....	96	Started asphyxia.
3.33.40	.....	90	
3.34.00	.....	60–140	
3.34.20	.....	76–150	
3.34.40	.....	80–134	
3.35.00	.....	70–150	
3.35.20	.....	76–130	
3.35.40	.....	90–130	
3.36.00	.....	70–140	

TABLE XXI. — *Experiment* 54. — Animal, dog; weight, 4 kilos.

Time. h. m. s.	Dose.	Blood-pressure. mm.	Remarks.
.....	.....	.....	Normal animal; sciatic prepared.
5.10.00	.....	106	
5.10.20	.....	100–110	
5.10.40	.010 gramme.	100–118	Injection into jugular begun.
5.11.00	.....	50–56	Injection into jugular ended.
5.11.20	.....	40–50	
5.11.40	.....	40–50	Weak faradization of sciatic.
5.12.00	.....	50–60	
5.12.20	.....	48–56	
5.12.40	.....	80–88	Strong faradization of the same nerve.
5.13.00	.....	70–76	
5.13.20	.....	94	
5.13.40	.....	100–110	
5.14 00	.....	100–114	
5.14.20	.....	102–116	

These results, therefore, indicate that hydrastine produces lowering of the arterial pressure in two ways,—by a direct action on the heart, and also through a paralyzing influence exercised on the vaso-motor system.

When the drug is injected directly into the carotid artery, there is noticed an immediate fall of the blood-pressure, which may be said to be due wholly to a vaso-motor influence, as the effect is produced undoubtedly before the heart is reached. This is shown in the following experiment:

TABLE XXII.—*Experiment* 54*a*.—Animal dog; weight, 12 kilos

Time. h. m. s.	Dose.	Blood-pressure. mm.	Remarks.
.....	.....	.....	Normal animal; left carotid connected with kymograph.
2.15.00	.....	102–142	
2.15.30	.015 gramme.	100–140	Injection into right carotid artery begun.
2.15.40	.....	94–124	Injection ended.
2.15.50	.....	86–118	
2.16.00	.....	64–98	
2.16.10	.....	52–88	
2.16.20	.....	46–80	
2 16.30	.....	40–78	
2.16.40	.....	36–78	
2.16.50	.....	36–78	
2.17.00	.....	32–70	
2.17.20	.....	40–80	
2.17.40	.....	40–80	
2.18.00	.....	40–76	
2.18.20	.....	40–76	
2.18.40	.....	44–82	
2.19.00	.....	50–82	
2 19.20	.....	52–86	
2.19.40	.....	52–90	Killed with chloroform.

A very interesting question arises now. Is this vaso-motor influence centric or peripheral? For the present I am inclined to believe that it is centric, owing to the fact that the arterioles do not seem to suffer any change until late in the poisoning, and it is then that they appear to be widely dilated. I have observed this late relaxation in the web of the frog's foot, under the microscope with the aid of the micrometer; but whether ultimately the blood-vessel walls or the vaso-motor nerves themselves are affected, it has not been accurately determined. However, there is strong evidence, in the course of my study, to show that the centric vaso-motor system is chiefly influenced by the alkaloid.

On the Respiration.—It has been intimated that hydrastine is a powerful depressant of the respiratory function, and proven precisely that it kills by failure of the respiration.

The drug, however, in moderate doses, produces at first an increase in the number of the respiratory movements, followed by a decrease, and, if the amount of the drug has been sufficiently poisonous, by a final cessation of the function under consideration.

This increase is due probably to a stimulation of the peripheral vagi, as such a result was not observed after the pneumogastrics were divided.

A good example of this primary action of hydrastine in the normal animal is given in the following experiment, but the cause was not fully determined.

TABLE XXII.—*Experiment* 55.—Animal, dog; weight, 4½ kilos.

Time. h. m. s.	Dose.	Respirations per minute.	Remarks.
1.30.00	.....	45	Normal animal.
1.30 20	.....	42	
1.30.40	.....	42	
1.31.00	.05 gramme.	39	Injection into jugular begun.
1.31.30	.....	50	Injection into jugular ended.
1 32.00	.....	52	
1.32.30	.....	58	
1.33 00	.....	46	
1 33.30	.....	38	
1.34.00	.....	32	
1.34 30	.....	22	
1 35.00	.....	18	
1.36.00	.....	22	
1.37.00	.....	27	
1.38.00	.....	27	
1.39 00	.....	29	
1.40 00	.....	29	
1.41.00	.....	34	
1.42.00	.....	33	

On Temperature.—Hydrastine, in small doses, does not seem to affect the temperature in the normal animal; but large and poisonous quantities reduce it to an appreciable extent, as is shown in this experiment:

TABLE XXIII.—*Experiment* 56.—Animal, dog; weight, 5 kilos.

Time. h. m. s.	Dose.	Rectal temp. C. scale.	Remarks.
12.20.00	.....	38.20°	Normal animal.
12.25.00	1.5 gramme.	.....	Injected hypodermically.
12.40.00	.....	38.5°	
12.55.00	.....	37.15°	Vomits white frothy mucus.
1.10.00	.....	37.5°	
1.25.00	.....	37.15°	
1.55 00	.....	38.15°	Has a tetanic convulsion.
2.25.00	.....	38.20°	

On the Pupil.—The drug, when given hypodermically or intravenously, produces no apparent change in the pupil. Locally applied, however, the alkaloid causes at first (due undoubtedly to reflex irritation) contraction, followed after a time by a dilatation of the pupil.

On the Glandular System.—Hydrastine produces, even in moderate quantities, an appreciable increase of both the salivary and the biliary secretions. With regard especially to the latter effect of the drug, the results of my

experiments are confirmatory of those obtained by the elaborate researches of Rutherford.*

CONCLUSIONS.

I shall now give a *résumé* of the conclusions which I have been led to adopt from the foregoing study:

1. Hydrastine is poisonous to both cold- and warm-blooded animals.

2. The minim fatal dose of the drug in the common frog (*R. esculenta*) is .001 gramme for every thirty grammes of the animal's weight.

3. The minimum fatal dose of the alkaloid in the dog, by hypodermic injection, is .50 gramme for every kilogramme of the body-weight.

4. Hydrastine destroys the irritability of the muscular tissue.

5. The alkaloid likewise destroys the excitability of the efferent or motor nerves.

6. Very large quantities produce loss of the functional activity of the efferent or sensory nerve-fibres, and also cause anæsthesia when locally applied.

7. Hydrastine, in small amounts, increases reflex activity by stimulating the spinal cord.

8. Later in the poisoning, by large quantities, hydrastine diminishes reflex action by stimulating at first Setschenow's centre in the medulla oblongata, and afterwards abolishes it by paralyzing the spinal cord.

9. The paralysis produced by the drug is due to an action upon the muscles, the motor nerves, and spinal cord.

10. The convulsions of hydrastine are of a spinal origin.

11. Hydrastine destroys the electro-excitability of the cardiac muscle.

12. The alkaloid, in small doses, produces a primary frequency in the pulse-rate, due probably to a stimulating action on the cardiac motor ganglia.

13. In moderate and poisonous amounts it diminishes the number and increases the size of the cardiac beats by an action upon the intracardiac ganglia and the heart-muscle itself.

14. Hydrastine lowers arterial pressure by a direct action on the heart, and also through a paralyzing influence exercised upon the centric vaso-motor system.

15. The drug produces at first an increase, and afterwards a decrease, in the number of the respiratory movements.

16. Hydrastine kills by failure of the respiration.

17. The alkaloid lowers bodily temperature.

18. The drug increases peristalsis.

19. In hydrastine-poisoning the salivary and the biliary secretions are largely increased, especially the latter.

20. Hydrastine locally applied produces at first contraction of the pupil; afterwards dilatation of the same.

(To be continued.)

* *British Medical Journal*, vols. i. and ii., 1879.

THE TREATMENT OF TUBERCULAR LARYNGITIS.†

By C. P. Ambler, M.D.,‡ Asheville, N. C.

IT is only with the advent of the operative procedures of Heryng and Krause that the curative treatment of tubercular affections of the larynx can be said to have been established.

By this I do not mean to say that tubercular processes of that locality never were healed, or were not aided in their healing, by our previous means, for we know that, even without any intervention of the healing art, nature has effected cures. Such cases were, however, the rare exception, and the various local applications seldom amounted to more than palliation.

Recently our resources, outside of operative measures, were enriched by Professor Koch's discovery of a remedy which acts specifically upon tubercular tissues, and particularly the laryngeal affections, where its action could be observed under the eye, were at once pointed out as the most favorable for the employment of his method.

Six months have now elapsed since its first employment, and while a number of cures are on record as undoubted evidence of the value of his discovery, in a much larger number the remedy seems to have failed, in part or entirely, and our great hopes that it would supersede all other means, both operative and palliative, are no longer justified by the accumulated experience of the best men in their special field of labor: and while its true position as a curative agent is being established, we must, as before, bring to our aid such other means as our experience justifies, especially so in cases where the remedy of Koch

† Read before the Buncombe County Medical Society Asheville, N. C., April 6, 1891.

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either seems to fail, or where other means can prepare the way for its successful employment.

It is not the object of this paper to deal particularly with results obtained from Koch's method, not enough cases having come under my observation for such a purpose, and those which I have observed were, with few exceptions, cases far advanced in tubercular disease of the lungs, and the laryngeal affection had also reached an advanced stage.

It may, however, be interesting to mention the effect of the remedy in those, comprising six cases, of which four were well advanced, both in the pulmonary and laryngeal affections, and two cases were in an early stage.

J. R., aside from his pulmonary disease, presented, upon examination, infiltration and swelling of the right arytenoid cartilage and slight infiltration of the posterior commissure. He was admitted to the Winyah Sanitarium January 14, and placed upon the Koch method of treatment.

His larynx, except some temporary congestion after the small doses of lymph used in the beginning, showed no permanent or important change until February 8, after six milligrammes had been given him on the previous day. During the night he suffered severe pain, and deglutition became very much interfered with. Upon examination, a number of miliary tubercles were found upon the previously involved right arytenoid cartilage; a few were also seen upon the left, and the swelling and hyperæmia were more intense.

These miliary bodies gradually disappeared in the course of ten days, and with them the swelling, leaving an unbroken surface, and the infiltration became so reduced that, on the 24th of February, the larynx was pronounced entirely normal.

He has since received injections up to .025 gramme without any further change in the larynx; the local condition of the lungs has also made great progress for the better, cough and expectoration are almost absent, and a steady improvement in flesh and strength goes hand in hand with the continuance of the remedy. The tubercle bacilli have also gradually and steadily diminished.

Another case is that of Mrs. E., who received local treatment for her tubercular laryngitis at my hands for some months previous to the administration of Koch's lymph. There was also slight infiltration of both arytenoids, and lactic acid applications improved the hyperæmia and seemed to hold further advance of the disease in check. Injections with Koch's lymph began on January 1, 1891, and the patient reacted in her larynx after .003 gramme was reached. A number of local reactions followed, with the usual temporary hyperæmia and swelling.

After March 14 no further reactions in the larynx occurred, and the infiltration has since entirely disappeared.

These are the only two early-stage cases of laryngeal tuberculosis who have been subjected to the lymph treatment, and in these the results are entirely satisfactory; indeed, it may be said that they are apparently cured.

It is, however, much different in the more advanced cases. The dosage in these, on account of the also advanced pulmonary tuberculosis and the depressed general health of the patient, had to be very small, only .003 gramme being reached. Owing to considerations outside of the laryngeal disease, the Koch method was suspended in three cases, and the patients put upon other management. Typical local reactions had been noted in all.

In one case some reduction of an infiltration of the posterior commissure did occur. Otherwise it cannot be said that the treatment had any material influence upon the laryngeal or lung-disease, nor upon the general condition of the patient, and it was given up because Dr. Von Ruck, the director of the institution, believed that better results would follow our old methods, and our subsequent experience proved this to be so.

I come now to the consideration of other methods of treatment, which are either curative or palliative.

When the pulmonary disease is far advanced and apart from the laryngeal affections, permanent arrestment of the disease is improbable or impossible, no procedures which are very painful and are attendant with subsequent suffering should be adopted, unless something material is thereby to be gained, either in relieving symptoms, or for the prolongation of life.

It is, under such conditions, difficult to say where the curative treatment ends and the palliative begins, neither are the measures we employ so radically different but what one or the other may come into use as a palliative or for a curative purpose, especially if we leave out of the question extirpation of the larynx, or laryngotomy, for the radical removal of the affected parts.

The object of the curative method is to remove or destroy tubercular tissue, either direct or indirect, and to bring about cicatrization.

In early-stage cases where the infiltration is limited the prospects from Koch's method seem good; but, apart from its employment, we have other means which have produced satisfactory and lasting results. Foremost among these stand the operative procedures with the curette, punch, and double-cutting curette, as employed and described by Heryng and Krause.

It is not probable that in their application all tubercular tissue is removed. Any one who expects to do that could not be satisfied with less than total extirpation of the organ. With the curette we break down the deposits and remove the proliferations, and set up an increased nutritive process during the reaction following the procedure, leading to cicatrization. Remaining tubercular tissue is either thrown off during the process of repair, or, with and after cicatrization, it undergoes pressure atrophy and absorption, or both.

When the larynx is entirely or extensively involved, when the deposits, ulcerations, and proliferations are beyond our reach, even in part, but particularly when, by the concomitant advance of lung-disease and other complications, the increased nutritive changes after operative procedures cannot take place, cicatrization will, of course, not follow, and by operation we not only gain nothing, but leave our patient the worse for our interference.

In a properly-selected case, however, we remove at successive sittings portions of infiltrated areas with the double curette or punch. This, of course, is done under cocaine and with the aid of the mirror, hemorrhage being slight, and generally easily controlled by applications of a strong solution of lactic acid upon a cotton-wrapped probe. According to the locality operated upon, it becomes more or less painful, the pain and soreness lasting from twenty-four to thirty-six hours. These slight operations are followed by moderate swelling and inflammatory reaction, which disappear in the course of some forty-eight hours; the lesion heals readily, leaving a pearly-white cicatrix. The operations are repeated at intervals of five or six days, until all the accessible infiltrations and proliferations are removed. Ulcerations which show no disposition to heal are scraped and treated with lactic acid, ten to eighty per cent., the latter being applied and rubbed in with a cotton-wrapped probe.

The most difficult to manage are the often enormously-thickened infiltrated cords; indeed, it must be confessed that our present resources are inadequate to do anything curative with them, and it is to be hoped that, if not Koch's, it may be Liebreich's remedy which will come to our aid in such cases.

The infiltrations and proliferations frequently present, difficult to see, and more difficult to reach, involving structures below the cords, will ever be a trial to the operator or him who wishes to make direct applications; besides, to do anything in that locality requires a patient who can bear prolonged manipulations. Lactic acid upon the cotton-wrapped probe, after cocaine, can be thoroughly applied, but operative measures will always be restricted.

When by such means we have been able to, so to say, "clear out the larynx," and have obtained cicatrization, the case may be said to be cured, at least apparently, and I have rarely seen relapses until, from the advance of tuberculosis in the lungs and other complications, the general nutritive process became seriously impaired.

Palliation is more frequently the object of our local treatment, and the earlier-stage cases, where we can hope to cure, are not so often seen in our institution as are those who show extensive involvement and destructive processes. Similar changes, as a rule, accompany them in the lung, and the treatment of the larynx has for its object the relief of cough, of pain, especially upon deglutition, and occasionally the removal of stenosis. For the latter, in a patient not entirely exhausted, the cutting curette can generally accomplish all that is necessary, and is far preferable to tracheotomy. This should not be thought of, except under extreme circumstances and in cases which absolutely cannot tolerate intralaryngeal operations.

When the ulcerations are not too extensive, lactic acid, and sometimes menthol, applied with a cotton-wrapped probe to the surface, considerable friction being used, may for a time control or even produce temporary improvement; but, in extreme cases, we have nothing that can equal frequent applications of cocaine, either alone or combined with iodoform and morphine.

Towards the end even this will have to be given up, and the exhibition of codeine and morphine are now, as ever, our only means of preventing unnecessary suffering.

Either as aids or as soothing measures, during a course of operative procedures and the later palliative stage of treatment, the va-

rious sprays, cocaine applications and inhalations, according to the exigencies in the particular case and the choice of the operator, are useful in conjunction, and can seldom be entirely dispensed with.

A case of interest in connection with this paper is that of Miss H. C., which came under our notice early last summer. Patient had been aphonic for two years.

The larynx was extensively involved, and a speedily fatal result threatened, not as much from the lung as from the throat affection, on account of extreme stenosis.

Not having Krause's set of instruments, we referred the case to a New York surgeon, who, however, only made a tracheotomy, and returned the case to us. She arrived here almost suffocated, and, upon examination by Dr. Von Ruck, it was found that the inner tube had been left out, and that a large mass of granulations projected into the laryngeal opening of the tube *in situ*, thus practically strangling the patient. The tube was promptly removed, as was also the mass of granulations, and subsequently matters went on so well that much of the swelling in the larynx subsided, the voice reappeared, and the tube could be dispensed with.

Some four months later the symptoms grew worse again, the stenosis returning, almost to the extent noted before tracheotomy. In the mean while a set of Krause's instruments had been procured from Germany, and the removal of the obstructing infiltrated swelling of both arytenoid cartilages and the ary-epiglottic folds was undertaken, as heretofore described. The lumen was extremely narrow, the masses entirely overlapping the cords. The breathing became very much better, even after the first operation, and now, after three operations upon each side, the cough, painful deglutition, swelling, and infiltration are very much improved, each removal of tissue being followed by prompt cicatrization and diminution of the swelling. There still remains upon the posterior wall below the cords a previously unsuspected proliferating tubercular mass, which the resulting contraction following the local application to it of cocaine shows is the only hinderance to the recovery of her voice.

At the time we began the operative procedures she had been readmitted, seeking the advantage of Koch's remedy, which Dr. Von Ruck was unwilling to apply under the condition of stenosis which was present.

Our efforts secured all the room required or thought requisite for the employment of the lymph, and we now wait its action upon the tubercular mass upon the posterior wall before attempting the there very difficult operation of its removal.

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*THE LITERATURE OF MEDICINE.**

By Schuyler C. Graves, M.D., Grand Rapids, Mich.

LADIES AND GENTLEMEN :—In the selection of a suitable subject for the annual address of the retiring president of our Society, I have deemed it fitting to choose that which, while not devoted to any of the specific subdivisions of the *ars medica*, would yet permit a broad, though, of necessity, a cursory, survey of the science and art of medicine, as viewed from a purely literary stand-point ; in short, the literature of medicine,—its origin, its progression, its present status, and its future probabilities.

1. *The Origin of Medicine.*—What year witnessed the birth of medicine? How and where did it come into existence ? Who was the first practitioner ?

These are questions which are difficult of solution. But let us examine the matter more closely.

Passing through the mediæval ages without pausing, we find evidences of medical knowledge in the Roman civilization as far back as B.C. 200. Proceeding to the older civilization of the Greeks, whence Roman ideas mainly emanated, we still find the dissemination of medical facts. Going still further to the hoary antiquity of the early Egyptians,—B.C. 1000,—we find the medical art being practised, and there is authority for the statement that the Chinese medical code was in existence four thousand years before the birth of Christ.

Who, indeed, can prove that medical men did not thrive among their compeers in the civilization of the Platonic Atlantis, whose antiquity transcends to so great a degree that of hoary Egypt or venerable China.

The medicine-man of the American Indian has had handed down to him from foregoing generations the scanty medical knowledge which he possesses. Did it come originally from that self-same Atlantean civilization, or is it the empiric enlargement of an ancient, initial intuition ?

* An address delivered before the Academy of Medicine of Grand Rapids, Mich., by the retiring president, Schuyler C. Graves, M.D., February 2, 1891.

All knowledge in regard to the origin of medicine must of necessity, therefore, be purely speculative. Medicine passes beyond the utmost limit of history, and merges into the fabulous era of prehistoric times.

There can be no doubt, however, that as long as man has been upon the earth, whether in a primitive or more developed state, disease has been a ravager, and if disease has existed, general remedies for the same, and the ability to manifest some discretion in their selection and use, have also obtained, call it knowledge, intuition, instinct, or what you will.

Observation of the lower animals teaches us the presence of a natural discrimination in certain emergencies. The domestic cat and dog, when in a state of health below par, and hence in need of certain reactive forces, show no hesitancy in going to the right plant for relief, not perhaps in all cases, but in a sufficient number to render evident the relation which exists between disease and instinct.

Can this instinct be limited to the animals specified?

What year, then, witnessed the birth of medicine?

I answer, the same year that witnessed the birth of primitive man, or, if we accept evolution, the same year that witnessed the birth of the first man-typifying and man-evolving organism.

How and where did it come into existence?

It came as the result of natural instinct which the Creator implanted in the animal organism at the start, and the place of its first manifestation was, of course, the location of the first instinctive animal.

Who was the first practitioner?

As instinct must have prompted the administration of the first dose, so the organism which gave expression to this instinct must have been the first practitioner. It may have been our ancestral clam. It may have been the first of primitive men.

2. *The Progress of Medicine.*—It is very evident to the most casual observer that, although we owe our start in medical knowledge to instinct, very few people of to-day would trust their lives, or the lives of loved ones, to the care of a physician who relied wholly upon the stock of instinct which nature had vouchsafed him.

This needs no comment, but it shows that medicine did not remain an instinctive practice. It grew; it developed.

Primitive medicine looked upon disease as an entity, an evil spirit, and those persons who had had experience in ridding the sick of their maladies being deified, temples were erected and priests ordained for the purpose of beseeching these canonized medical saints to cast out the evil ones. Later disease was supposed to be due to the anger of the gods.

For these two reasons, if for no others, there arose superstitious rites and incantations for the cure of the infirm, such as we know take place to-day in all sincerity among certain Indian tribes and in the negro settlements of Central Africa.

Thus we come to learn why the priest and physician were one and the same person in the times referred to, for medicine at that period was oracular, the authority for the superstitions and incantations being derived, through the agency of the medico-priests, from the oracles of the deities.

Superstitions, in one form or another, either in the guise of astrology, alchemy, or wild philosophical vagaries, continued to cling to medicine—that is, to civilized medicine—for many centuries, and the *ars medica* was not purged of them until the sixteenth or seventeenth century.

However, the first objects of sensible attention were cleanliness, hygiene, and the prevention, as far as possible, of contagion, and the first scientific remedies were regulation of the diet, application of water in shape of baths (hot or cold, impregnated or not with minerals), and decoctions of roots and herbs.

Later the sick were in the habit of lying by the wayside in order to receive attention and treatment from those of their fellow-creatures who had suffered from the same maladies and had been restored to health. Be it also known that no wayfarer was allowed to pass any sick person thus exposed on the highway without questioning him in regard to his infirmities.

When recovered, these patients were required to record in the temples their symptoms and the remedies used.

Thus grew up a vast storehouse of practical information on the natural history and cure of disease, affording a basis for modern pathology and therapeutics.

It will be interesting to relate in this connection that the faith which was reposed in the validity of this congeries of medical facts was so strong that any physician who followed the dicta therein contained was held in honor, whether death followed his dosing or not; but if he were detected in making any innova-

tions, or in departing to the slightest degree from the written law, he was punished with death, even if his patient made a perfect recovery.

In looking over the annals of Egyptian medicine, we find much that is interesting and instructive.

Specialists existed in those days. The eye, the ear, the teeth, the stomach, each had its own particular votary.

Dietetics, also, was carried to quite a degree of perfection, only *so much* of particular varieties of food being allowed.

As the Egyptians abhorred dissection, their knowledge of anatomy and physiology was of necessity very limited, as, for instance, the belief that the heart grew two drachms each year until the fiftieth, after which it decreased in the same ratio; but to say that they abhorred dissection does not at all express their feelings in regard to the sacredness of the dead human body.

Their ideas on this subject were so strong that they would curse and chase and pelt with stones the very men whose office was to remove the viscera from the body preliminary to the process of embalming, so that these unfortunates, for doing a most important, yea, an indispensable, as well as a religious act, were compelled to watch their opportunity, hasten through with their work, and then run for their lives.

We observe that by the system of recording medical facts and experiences practised by the Egyptians much was learned that was true. In short, a gain was made, and medicine progressed under early Egyptian nurture.

Let us now glance at medical knowledge and practice in ancient Greece.

About B.C. 1000 there came upon this world, either in fact or in fancy, that personage or mythological character known as Æsculapius, and called the god of medicine. Whether he really had an existence or not is a moot question. There is considerable doubt about it, but it is said that he lived, and that he was the father of many descendants, all the male representatives of whom practised medicine under the appellation of the Asclepiadæ.

"History repeats itself."

Romulus, the founder of Rome, was suckled by a she-wolf. Æsculapius, his illustrious predecessor, was suckled by a she-goat. Romulus had a foster-father in the person of a shepherd; so had Æsculapius in that of a goatherd.

In his treatment of the sick Æsculapius is said to have invoked the powers of the gods, and to have supplemented these invocations by a vigorous use of the medicines of the day,—decoctions for internal use and macerated herbs for external application in the arresting of hemorrhage and the soothing of pain.

In regard to the skill and success of Æsculapius as a practitioner, hear what Dunglison, in his "History of Medicine," culls from Pindar, the lyric poet of Thebes, concerning him:

"Those whom nature made to feel
Corroding ulcers gnaw the frame;
Or stones far hurl'd, or glittering steel,
All to the great physician came.
By summer's heat, or winter's cold
Oppressed, of him they sought relief.
Each deadly pang his skill controlled,
And found a balm for every grief.
On some the force of charmed strains he tried,
To some the medicated draught applied;
Some limbs he placed the amulets 'round;
Some from the trunk he cut, and made the patient sound."

Reference can be observed in this Pindaric strain to the invocations of Æsculapius, previously mentioned, and also to his treatment of wounds and ulcerations.

But now let us look more particularly at the general state of medicine in ancient Greece and its progress.

The medical art was at first hereditary, as touched upon before in the statement regarding the Asclepiadæ, and its secrets were not to be divulged. Knowledge was exceedingly limited, and ignorance correspondingly great. The recovery of a patient, for instance, was a monument to the professional skill of the practitioner; but his death was ascribed to want of confidence in the physician or to lack of obedience to the commands of the gods.

Anatomical knowledge in the time of Æsculapius was very contracted, the Grecian argument against the practical study of the dead being that, inasmuch as the soul after death was compelled to wander on the banks of the Styx until the earthly casement had received the rites of pagan cremation, all haste was to be made, as soon as a relative or friend had died, to dispose of his body after this fashion, and such action was looked upon as an imperative duty.

The ancient Greeks had a "divine old man," the so-called "father of physic," progressive Hippocrates. This medical savant, the second of that name, lived about B.C. 400; but he was far in advance of his age.

Hippocrates, considering everything about him and the time in which he lived, was a marvellous worker for the advancement of medical knowledge. He separated medicine from philosophy, and based it upon rational experience; he took that which was good from previous accumulations, and repudiated that which was bad; he started original investigation; he commenced practical work in anatomy by dissecting animals, chiefly the dog and pig, and then reasoned out human anatomy by analogy. His maxim was, "Nature, the first of physicians." His mistakes were many, but his path lay in the right direction. His works, quite a number of which have come down to us, may or may not be authentic, for, being traced first upon waxen tablets, transferred thence to the untanned skins of animals, thence to papyrus, and, finally, after the invention of the printing-press, to paper, we cannot tell how many interpolations may have been made, and hence are oftentimes unable to decide which is genuine and which spurious.

Passing along in Grecian history to B.C. 300, we find a physician, Praxagoras by name, who pushed medical knowledge a step nearer the truth by discovering the difference between the arteries and the veins; but he never even dreamed that these vessels contained blood. He only noticed that the arteries pulsated and the veins did not.

The word *artery* signifies *air-vessel*, and up to the time of Praxagoras this same word had been used to designate the trachea. Why did he apply it to one class of blood-vessels?

There are two reasons for this application. 1. The artery pulsated. This was supposed to be due to a vital force residing in the vessel-walls, and air at that time was considered the seat of vital force. 2. After death the arteries were always found empty, and hence to all appearances full of air.

About the time of Praxagoras (B.C. 300) the first human dissections were made by Herophilus, a Greek, under the sanction of Ptolemy Philadelphus and Ptolemy Euergetes, in Alexandria, which at that time was the centre of terrestrial knowledge; and this same Herophilus, by the way, discovered that the pulsations in an artery were not due to inherent vital force, but to the contractions of the heart.

Passing now to Roman medicine, we find that it was introduced by freedmen from Greece, who had picked up a little knowledge on the subject at home. Later better men filled the ranks, among whom may be mentioned Celsus, the medical Cicero, contemporary with Tiberius, and Galen, the Roman Hippocrates, contemporary with Adrian.

Not much difference is noticeable between Roman and Grecian medicine, and hence we move on to later eras.

Coming down to the seventh century (A.D.), we find medical schools established in England. In the eighth, the Arabic school began to flourish, and to the school of Arabia pharmacy and chemistry are indebted very much. Indeed, to so great a height, considering the times, did Arabic and Moorish medicine rise, that, as I have stated in a former paper, with the completion of the conquest of Granada by Ferdinand the Catholic, the Spanish peninsula, in consequence of the departure of the expatriated Saracens, was plunged into veritable scientific darkness.

Until the twelfth or thirteenth century the affiliation between priest and physician was kept up; but at that time (or thereabouts) monks were forbidden to practise the art of medicine both in France and in England, although the influence of the union was still observed in the fifteenth century, when physicians, after the manner of monks, were compelled to devote themselves to celibacy.

The pseudo-science of astrology was also connected with medicine even until the eighteenth century.

Illustrative of this connection, I quote from an old work in my possession, written by a Dublin physician in 1748.

Writing of a medical case in his practice, the doctor says,—

"Then I advised bleeding eight or ten ounces on the 7th of November; that on the 8th the purge should be repeated, *because the new moon was the next day;* for the eminent Dr. Mead and other skilful authors have rightly observed that these kind of diseases grow worse about that time."

The patient having been advised to take a course of sea-bathing, the doctor continues:

"After the fourth time of going into the sea he was much better, although *this night being full moon*, he grew a little worse;" but in time "he came from bathing daily brisker and stronger, and readier in expressing his words. Neither on the ninth (9th) of the month, *though the new moon was at hand*, had he any convulsions or trembling, or the least increase in any symptom of his distemper."

The time of the new or the full moon, it is thus seen, was supposed to be unfavorable to convalescence.

It might, also, at this juncture be interesting to quote a portion of a law governing the actions of medical men in France during this century.

"If a physician shall wound a man of noble birth, he shall pay a fine of one hundred sous; and if the gentleman shall die of the effects of the operation, the physician shall be delivered up to the relatives of the deceased, who may treat him as to them seemeth mete; but if it be a serf whom he has wounded, or caused the death of, he shall be made to restore another to the lord."

I have said before that the first human dissections were done by Herophilus in Egypt some three hundred years before the time of Christ. This is true; but the practical study of human anatomy was not kept up, later medical men, until the Middle Ages, gaining their knowledge of anatomy from the notes of preceding anatomists, Galen particularly, and also a few others, who had dissected numbers of the lower animals; but human dissections began to be made openly in the fourteenth century by Mondini de Luzzi, professor of anatomy at Bologna, who wrote a work on anatomy that was considered classical for two centuries.

It was at that time, and still is to-day, the practice of professors of anatomy to have their subjects dissected, in part, of course, prior to demonstration before their pupils, by persons known as prosectors, and it is strange to relate that the first prosectors were barbers' apprentices, who used their razors in the work.

From this as a starting-point we soon observe barbers in medicine. Perhaps, logically, it was reasoned that, insomuch as anatomy was the basis—the *a*, *b*, *c*—of surgery, and barbers' boys were employed in anatomical work, the full-fledged barber must have within his jurisdiction the art of the surgeon. At all events, for several centuries after the age of Luzzi barbers practised surgery, commencing with venesection and the administration of medicated baths, passing into wider fields, and some of them even acquiring the proud distinction of being barber-surgeon to the king.

The well known barber-pole of to-day is but a relic of its master's former glory as a blood-letter, the white band typifying the constricting fillet and the red the blood, which poured forth its crimson flood at the lancet's touch. The union of scissors and bath-tub in the sumptuous tonsorial apartments of the modern metropolitan hostelry is likewise a relic.

These barbers, who, as a rule, were extremely ignorant, continued their association with medicine until the middle of the eighteenth century, when they were tabooed and relegated to the sole practice of the art of the *tonsor*.

The invention of printing in the fifteenth century did a great deal for the progress of medicine, and that of gunpowder did the same for the surgical branch of the art, although in a very different sense. Gun-shot wounds were something new. The ancients had seen nothing of such injuries, and hence, of necessity, were quite silent on this point in their medical writings.

On this account the surgeons of the middle ages, brought face to face with new surgical conditions, were compelled to depend upon their own ideas for proper treatment.

This, of course, developed the art considerably.

In the sixteenth century a final divorce took place between chemistry and alchemy, and the former from that time has rested upon a secure foundation.

The progress of medicine was very rapid during the two or three centuries which precede our own times, notable points in medical discoveries being confined to no single branch of medicine.

The discovery of the circulation of the blood in the early part of the seventeenth century by William Harvey, physician to James I. and Charles II., was a long step forward, and who can estimate the value of the thousands of lives annually saved by Edward Jenner's discovery of the protective power of vaccination in 1798.

But the march of medicine has not been unsullied by the encroachment of error and fraud. The tar-water of Bishop Berkeley as a panacea was popular for some considerable time. So also were the metallic tractors of Perkins, who thought that the application of pieces of metal over diseased tissues would work a cure.

For a considerable period of time the weapon-ointment, or what was about the same thing, the famous sympathetic powder of Digby, was used with supposed efficacy.

This consisted in the application of a healing ointment or powder *to the instrument which had caused a wound*, thus curing the injury.

Scott, in the "Lay of the Last Minstrel,"

according to Dunglison, refers to this ointment when he writes,—

> "But she has taken the broken lance
> And washed it from the clotted gore,
> And salved the splinter o'er and o'er."

The mind-cure, the faith-cure, Christian (pseudo) science, etc., I simply mention as examples of fraudulent systems of medicine. There may be strands of truth in some of these "pathies," but to tie to they are unreliable, to say the least.

Errors, however, do not, as a rule, last long. Like the blue-glass craze, they have their day, blazing perhaps with some brilliancy for a while, but finally fading away, after a longer or shorter existence, like a candle dying in its socket. They join the army of their predecessors, and become the relics of a more or less superstitious past.

3. *The Present Status of Medicine.*—Medicine existed once in a rudimentary state, as we have seen. Has it arrived at perfection to-day? Not at all; but, nevertheless, enormous strides, on progressive lines, have been made, and now, through present knowledge and the cumulative experience of the past, thousands of lives are annually saved that hitherto would undoubtedly have been lost.

Let us glance briefly at what invention has done for the science and art of medicine.

As the telescope has brought nearer and for more accurate study the worlds which move in their grand orbits about us, so (1) the microscope has revealed all the hitherto unknown wonders and facts connected with the "unseen universe" beneath us.

Through the microscope the ultimate structure of our bodies has been ascertained and the physical constitution of all the body-fluids also made known. Not only by this means has health been studied, but disease likewise.

Through the microscope scientific experts have been enabled to ascertain many of the true causes of disease and the conditions upon which an enormous array of symptoms depend.

This, it is needless to say, opens the way for a more rational, and thus a more successful, treatment of our infirmities.

(2) The laryngoscope throws light, by the hand of the skilful operator, upon any lurking disease of the throat or larynx. (3) The stethoscope gives us the ability, so to speak, to look into the body through the external walls, and witness what is going on in the darkened chambers within. (4) The clinical fever thermometer shows us the slightest change in the patient's temperature; and (5) the sphygmograph, an accurate record of variations in the pulse-rate. We have to-day (6) the ophthalmoscope, which makes the interior of the eye read like an open book; (7) Esmarch's bandage, for the performance of bloodless operations upon the extremities; (8) intubation apparatus, for use in suffocative forms of laryngitis; (9) mouldable splints, for fractures; and (10) the pneumatic cabinet, for obtaining atmospheric differentiation in the abbreviation of pulmonary troubles.

Hygiene, or sanitary science, is to-day much more systematic and efficacious than ever before, chemistry has advanced wonderfully, new remedies, some of great value, are being brought out, and balneology figures largely in the therapeutics of hyperpyrexias. Diseases are often prevented, and thus the necessity for a cure and the danger of a death summarily abolished.

In the matter of drugs, there has been a fear, for the last few years, that the natural supply of quinine would soon fall far short of the demand; but some energetic, scientific German chemist has succeeded in making quinia (or quinine) by synthesis, thus preventing any possibility of scarcity and keeping down high prices. I need only mention chloroform and ether, the now indispensable agents, which bring freedom from pain, and a condition of blessed unconsciousness to those suffering from the indescribable tortures and agonies to which we mortals are, alas! too often subjected. Shall I forget, in this God-given list, to mention the beneficent cocaine? Not so; for by its use the physician forces to speedy flight the pain incident to minor surgical operations without abolishing consciousness in the slightest. Vaccination, previously referred to, should not be omitted in this connection, for we of to-day can never be brought to a personal realization of the horrors which visited the citizens of the Middle Ages when grim-visaged smallpox stalked through the land, and banished, with unspeakable agonies, thousands upon thousands of prostrated and abandoned individuals "to that bourne from whence no traveller returns."

Even to-day the immortal Jenner is being duplicated in the noble Pasteur, of France, who, it is confidently believed, will soon rob that great scourge—hydrophobia—of its horrors; and, as I pen these words, the intelligence is flashed throughout the civilized globe that the illustrious Koch is offering hopes of

relief to a world stricken with that great white plague,—consumption.

Let us all fervently trust that these hopes may, indeed, be realized.

Even in our own Michigan those sturdy investigators, Shurly and Gibbes, are doing some very encouraging work in the matter of tuberculosis.

I will not detain you by more than a passing reference, under this heading, to what antisepsis, as understood by modern science, has done for surgery. The surgical maxim, *Noli me tangere*, is almost a thing of the past.

The cerebral, spinal, thoracic, and abdominal cavities are now freely opened and explored, with the result of saving many lives.

4. *The Future Probabilities of Medicine.*—Lines developed in the past extend more or less deeply into the future, and although we cannot accurately foresee the status of medicine in the centuries to come, we can, by noting the drift of the times, realize how certain facts and principles, at present but dimly outlined, will undergo more perfect development. For instance, the matter of hypnotism.

Hypnotism is not a new thing. The ancient Egyptians in their Apis worship, the Greeks at the Delphic shrine, witnessed hypnotic manifestations on the part of the priests and priestesses, so that when Frederick Mesmer, towards the close of the last century, astonished at first Vienna and then all Europe, he merely reapplied an ancient principle.

Science having taken hold of the subject, we find that the true principle of mesmerism, stripped of all chicanery, comes forth as the modern hypnotism. It has also been ascertained that the hypnotic state is not to be brought about by any so-called "fluid," or by any impression passing from the hypnotizer to the hypnotized. The condition is a subjective one, being brought on by the patient assuming a perfectly passive state, and permitting one or more of his senses to be impressed by appropriate agencies, as, for instance, keeping the eyes steadily fixed upon some smooth, shining object, or allowing the filaments of the auditory nerve to be saluted by a monotone, such as the sound of a tuning-fork or a gong, provided, of course, that the passiveness be all the time maintained.

But I do not propose going into this matter in detail. I merely wish to state that in the not far distant future I believe much will be done through the agency of hypnotism. Certain mental and physical ailments will, no doubt, be benefited, and some cured.

Operations will be performed while the patient is under its influence, and some enthusiastic disciples even assert that wickedly-inclined youths will in this way be brought back to the path of virtue. This matter, however, passes beyond the medical and into the moral.

The great fact of future life, in its relationship to medicine, at all events, is the development of sanitary science. More of prevention and less of cure. The physician of the future will be paid to keep people from being ill, and not to cure them after they have become ill.

Some one has said that this is the custom among the Chinese physicians, and, if so, China, with all her old-fogyism, is far ahead of the otherwise progressive Western nations.

Sewerage, drainage, water-supply will all be arranged excellently well. Garbage and dead human bodies will be cremated, earth burial thus becoming a relic of the past.

Even surgery will participate in the onward march, for by continual improvements in the manufacture of labor-saving and life-and-limb protecting machinery, accidents will become alarmingly scarce. In fact, when we consider what has been done in and by medical science during the past quarter of a century even, it is difficult to keep from falling into the dream of Bellamy when we gaze into the future.

Is the millennium to be realized? If yes, then so much the better for the world and so much the worse for the doctors.

In closing this address I cannot refrain from reading, as peculiarly fitting, a brief poem by Dr. Holmes, composed for the meeting of the National Sanitary Association in 1860. It is as follows:

"What makes the healing art divine?
The bitter drug we buy and sell,
The brands that scorch, the blades that shine,
The scars we leave, the 'cures' we tell?

"Are these thy glories, holiest art,
The trophies that adorn thee best,
Or but thy triumph's meanest part,
Where mortal weakness stands confessed?

"We take the arms that Heaven supplies
For life's long battle with Disease,
Taught by our various need to prize
Our frailest weapons, even these.

"But ah! when Science drops her shield—
Its peaceful shelter proved in vain—
And bares her snow-white arm to wield
The sad, stern ministry of pain;

"When shuddering, o'er the fount of life,
She folds her heaven-anointed wings,
To lift unmoved the glittering knife
That searches all its crimson springs;

"When faithful to her ancient lore,
She thrusts aside her fragrant balm
For blistering juice, or cankering ore,
And tames them till they cure or calm;

"When in her gracious hand are seen
The dregs and scum of earth and seas,
Her kindness counting all things clean
That lend the sighing sufferer ease;

"Though on the field that Death has won
She saves some stragglers in retreat;
These single acts of mercy done
Are but confessions of defeat.

"What though our tempered poisons save
Some wrecks of life from aches and ails;
Those grand specifics Nature gave
Were never poised by weights or scales.

"God lent his creatures light and air,
And waters open to the skies;
Man locks him in a stifling lair,
And wonders why his brother dies.

"In vain our pitying tears are shed,
In vain we rear the sheltering pile,
Where Art weeds out from bed to bed,
The plagues we planted by the mile;

"Be that the glory of the past;
With these our sacred toils begin;
So flies in tatters from the mast
The yellow flag of sloth and sin,

"And lo! the starry folds reveal
The blazoned truth we hold so dear:
To guard is better than to heal,
The shield is nobler than the spear."

STUDIES IN THERAPEUTICS—CACTUS GRANDIFLORUS.

By John Aulde, M.D.,* Philadelphia, Pa.

CACTUS GRANDIFLORUS is a remedy which has recently been brought prominently to the attention of the medical profession through the publication of a large number of reports from physicians;† and as these reports correspond so closely with my own experience with the drug, I have deemed them of sufficient interest to warrant the preparation of a synopsis.

Two preparations found in the market are the fluid extract and the tincture, both of which are freely miscible with water. According to my own observations and the reports of those who have used the drug, the dose of either ranges from 5 to 10 or 15 drops, although the dose of the fluid extract is not given at such short intervals as the tincture. Gregory, who has used the tincture for more than fifteen years, recommends 5 drops every two, four, or six hours, but the fluid extract need not be given oftener than three times daily. A new preparation, cactina, has lately been advertised in the journals, which is probably an evaporated fluid extract, as it is offered in the form of pellets. While it is quite possible to prepare cactus in this form, there are the accompanying dangers of defects, due to the method of manufacture, and it should not cause the rejection of the remedy should this new product fail to afford the results claimed for the other preparations.

Cactus is distinctly a cardiac tonic, free from the so-called cumulative action of digitalis, and less objectionable to the palate than either nux vomica or strophanthus. It carries with it no narcotic effects, nor does it produce any material constriction of the arterioles, while it appears to possess valuable properties in regulating the movements of the heart, whether the irritability be due to "nervousness" from reflex causes, or to the presence of organic changes, features which will be developed more fully in the course of this review.

The remedy has proven serviceable in the treatment of dilatation with hypertrophy, accompanied by a murmur, in which case we may assume that the dilatation had increased more rapidly than the hypertrophy. In cases of palpitation, such as frequently occurs as a sympathetic functional disorder due to uterine troubles, or that which is a factor in indigestion with a relaxed (flabby) condition of the system, in which formication is a prominent symptom, cactus is indicated. These patients, when females, often complain of menorrhagia or metrorrhagia, and usually suffer more or less at the catamenial period. While cactus may be useful as a temporary expedient, it should be conjoined with other treatment directed to the stomach and the uterus. Thus, in the case of a disordered condition of the stomach, it may conveniently be combined with the digestive ferments, instead of strychnine or nux vomica.

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* Member of the American Medical Association; of the Medical Society of the State of Pennsylvania, etc.

† "The Pharmacology of the Newer Materia Medica." George S. Davis, Detroit, Mich., Part IV., February, 1890.

℞ Ext. cacti grandiflori,
Tr. nucis vomicæ, āā ʒii;
Liq. pancreatin., q.s. ad., fʒiii. M.
Sig.—One teaspoonful *with* meals.

Where we have to deal with metrorrhagia and other uterine affections, it may be safely and advantageously added to a prescription containing cimicifuga, ergot, or, in the case of leucorrhœa and endometritis, with or without subinvolution, it will be found beneficial to alternate it with calcium sulphide, to which should be added local treatment in the form of medicated tampons.

℞ Ext. cacti grandiflori,
Ext. cimicifugæ,
Ergotæ (normal liquid), āā ʒii;
El. aurantii,
Glycerini,
Aquæ partes æquales ad., fʒiii. M.
Sig.—One teaspoonful every four hours.

Not infrequently in young women, and in those who are married, we meet with palpitations which appear to be purely nervous, where it will be found that digestion is at fault, manifested usually by insomnia, although they take their meals regularly. In these cases diet must be regulated and certain objectionable food-substances prohibited, generally the starchy and fatty foods and sweets. Moderate exercise must be insisted upon, and proper attention given to the functions of excretion. If the skin be dry and harsh, the indications may point to the use of arsenic, rhus toxicodendron, or pilocarpine, all of which favorably modify digestion, while they promptly influence the activity of the skin.

In the case of dilatation, with anasarca and œdema of the extremities, with or without valvular disease, when there is apparently no sufficient reason for the persistence of the disorder, and when digitalis, diuretics, and cathartics fail to produce improvement, cactus promises to effect good results. This is the class of cases in which Bartholow recommends the employment of arsenical preparations, and occurs for the most part among persons advanced in years, where there is more or less atheromatous degeneration present, and where alcoholic preparations of digitalis result finally in bringing on sudden collapse and death. An examination of the urine shows an absence of albumen, although the specific gravity may be low, but, as a rule, the signs are negative. Here evidently is an indication for the addition of cactus to the arsenic, and, if there be a demand for catharsis, we have in apocynum an admirable remedy.

℞ Ext. cacti grandiflori, fʒii;
Fowler's solution, gtt. xxxvi;
Tr. gentianæ comp., q.s. ad., fʒiii. M.
Sig.—One teaspoonful in water every four hours.

Dr. O'Hara has reported several cases of hypertrophy, with dilatation and mitral insufficiency, in which cactus proved efficient after the failure of digitalis and other drugs. Dr. A. Orlando Jones (*Brit. Med. Journ.*, 1890) thinks cactus best adapted to the asthenic conditions, while he approves of digitalis in sthenic cases. Byrd recommends its use in subacute and chronic rheumatism, and in these instances it will be found advisable to combine it with rhus toxicodendron or with cascara when there is a distinct indication for the employment of a laxative aside from the action of the drug upon the heart. The value of cimicifuga should not be overlooked in these cases, as it will prove an acceptable adjuvant to cactus, and, besides, actæa is a useful drug in nearly all forms of rheumatism.

℞ Ext. cacti grandiflori,
Ext. cimicifugæ, āā fʒiss;
Tr. rhois toxicodendri, gtt. viii;
Glycerini, fʒss;
Tr. xanthoxyli, q.s. ad., fʒiv. M.
Sig.—Two teaspoonfuls in water after meals.

The cardiac irregularity and exhaustion due to morphine or chloral is promptly met by cactus. When these drugs are suddenly withdrawn from those accustomed to their use, it will be advisable to combine with the cactus moderate doses of fluid extract of coca and strychnine, and in quite a proportion of the cases the addition of cannabis indica will prove serviceable. Cases of sexual exhaustion are remarkably benefited by the exhibition of cactus, doubtless because it lacks those peculiar stimulating properties which it is so important to avoid. We are beginning to learn and understand that overstimulation is always followed by a period of depression. The action of cactus in these cases may be appreciably increased by the judicious exhibition of nux vomica, damiana, and phosphorus.

℞ Ext. cacti grandiflori,
Tr. nucis vomicæ, āā fʒii;
Ext. damianæ, fʒiv;
Glycerini,
Tr. gentianæ comp., āā q.s. ad., fʒiii. M.
Sig.—One teaspoonful after meals.

We are often confronted with patients who suffer from exhaustion, with irregular or intermittent pulse, due to the abuse of tobacco, and here, instead of unpalatable remedies like

nux vomica, we have cactus, which is rather agreeable than otherwise to most persons, and the effect upon the system and the circulatory apparatus is quickly apparent. The patient should take 5 to 10 drops three times daily. The same treatment is indicated for the relief of a similar condition, which often affects those accustomed to the inordinate use of tea. The active principle, theine, it has been found, will cause the heart to intermit, but in cactus we have a drug which meets this emergency, although I do not hesitate to say that the use of tea should be discontinued, and coffee or coca substituted.

The intermittent heart from the abuse of tea, accompanied by indigestion, with flatulency due to fermentation of food, may be greatly benefited by the alternation of gelsemium with cactus, with a view to relieve undue tension and favor the re-establishment of the secretions.

Gregory, of Yreka, Cal., believes cactus to be more valuable than digitalis where dilatation has outstripped hypertrophy, and says it is the only remedy he uses in functional valvular disease.

Engstad, of Grand Forks, Dak., says, "I now depend upon it [cactus] in preference to digitalis in functional disorders," but complains that many of the preparations are unreliable (THERAPEUTIC GAZETTE, September, 1890). He records its successful employment as a cardiac tonic in typhoid fever after the failure of strychnine and digitalis, and my own experience confirms his report.

Although aware that digitalis preparations enjoy a well-merited reputation for the relief of heart-troubles, I am of the opinion that many of the cases of sudden deaths from "heart-failure" may be traced directly to the injudicious employment of the drug; and I think the medical profession will hail with delight the appearance of a remedy which will in a great measure take its place, and bespeak for cactus a favorable reception and careful study.

4719 FRANKFORD AVENUE.

REVULSIVE MEDICATION.

BY HUBBARD M. SMITH, M.D., VINCENNES, IND.

YOUR editorial on "Counter-Irritants," in the January number of the GAZETTE, is one of interest and timely in this age of progress in the healing art; especially does it seem so when old-time methods are ignored and esteemed as mistakes of a past age. Although you do not espouse the views of the old fogies or the progressives of modern medical science, the concluding sentence embodies the central thought of the controversy when you say, "Experience rather than fine-spun theories must still decide the matter."

Theories are but theories, not facts, and are being overturned every year. One fact, proven by varied experience, is worth many theories, however plausible and seductive to the philosophic mind. The assertion that pneumonia is caused by a microbe has not been demonstrated satisfactorily. That microbes may be found in the sputum of patients suffering from pneumonia may be admitted, but that they cause the attack is another question. The lungs having become congested, and then inflamed by cold and moisture, would offer a fit soil for the microbe to vegetate in. Reasoning upon this subject, if it is admitted pneumonia is caused by a contagious microbe, we would have to admit that rubefacients and blisters would have little or no effect in arresting or curing the disease. But when a vast experience is brought to our aid to show that the disease may be beneficially affected by mustard, and other rubefacients and vesicants; nay, if applied early, with auxiliary treatment, may be aborted, then we must conclude that theory must stand aside for uncontroverted facts. That all internal inflammations can be beneficially influenced by rubefacients and vesicants applied over the seats of the disease cannot be successfully denied. For many years I have treated successfully inflammations of the internal organs with the free use of mustard as a prime auxiliary, and the benefit following its application is so universally appreciable that to my mind doubt is out of the question.

In catarrhal troubles with children, especially of the chest, I have found counter-irritants a sheet-anchor in the first stage of the disease. The assertion of the opponents of this course, that they are "useless," even "injurious," and "augmenting fever and suffering," is purely imaginative and bordering on a sickly sentimentality. Often have I been called to the bedside of little sufferers with congestion of the lungs, evidencing pain at each respiration, which was short, with great restlessness and fever, when they have been soothed to a sweet sleep in half an hour or less by a jacket of mustard-cloth, often sinking to sleep while the mustard was on them. To say that such treatment was cruel, useless, and calculated to augment fever is to

assert that which experience demonstrates not to be true. Two years ago I was called to see a brother physician who was suffering greatly from pneumonia and enlarged liver, and he had obtained no rest nor relief. I ordered a mustard-plaster large enough to envelop chest and extend partly over the abdomen. He expressed himself afterwards that the mustard treatment was a revelation to him; its influence was so prompt and marked that he abandoned his theories about rubefacients and blisters for substantial facts. One trouble with the profession as well as the laity in the use of these agents is that they are too sparing with them. To be of material benefit, large plasters must be used, and for effect, not merely pretence in a routine way. I confine my remarks in this article as referring mostly to children. When the child is very young, when I have occasion to use mustard, I order two tablespoonfuls of the strongest mustard (ground) to a pint of boiling water, and then have a cloth, sufficiently large to envelop the whole chest, dipped in this and wrung out so as not to drip when it is wrapped around the child, and a warm, dry cloth is placed over; better if a rubber cloth or oiled silk is used. This application is repeated soon again, unless the surface is very red; and when the redness begins to fade the application is repeated. In many cases the congestion never eventuates into inflammation under this treatment, and soon the patient is convalescent. If this plan be pursued early and rigorously, blistering seldom becomes necessary. But in adults, even when the inflammation was passing through its stages, when the patient's case seemed in a balance, and when suffering was acute, I have witnessed quick and permanent relief follow a large blister, followed with an emollient poultice.

This is a part of my testimony in favor of rubefacients and blisters, after nearly fifty years' experience.

A NEW METHOD OF INDUCING PREMATURE LABOR.

Dr. Schrader, of Hamburg, publishes in the *Centralblatt für Gynäcologie* a method of inducing premature labor based on his observations that cold is a greater excitant of the nervous, and consequently also of the muscular, system than warmth. Continuous irrigation at the temperature of 45° F. is impracticable, on account of the pain it causes, but a cold douche, alternating with a warm one, can be borne. Dr. Schrader connects a vaginal glass tube by means of a T-shaped piece and the necessary india-rubber tubes to two irrigators, one of which contains the cold and the other the warm water. By allowing now one instrument and now the other to work, cold or warm water may be sent through the vaginal tube into the vagina. Two people are required,—the one to fill the irrigators, the other to work the douche. For each sitting about twenty-four litres of cold and half the quantity of warm water at 112° are required, and the douche has a fall of about one metre and a half. The irrigation begins with the warm current, and before the cold water is turned on pressure is made on the perineum with the vaginal tube, so as to allow all the warm water to run away from the vagina. The same plan is observed before the change from cold to warm, by which means the alteration in the temperature, as felt by the patient, is always sudden. Each time about two litres of cold and half the quantity of warm water are used. The douche is generally repeated about every hour and a half until labor is active enough to make its continuance probable. Of eighteen women treated by this method exclusively, and four others who were partly so treated, one died of eclampsia twelve hours after delivery, but all the others made a good recovery. The eighteen women who were treated by the douche exclusively had twenty children, of whom fifteen—that is, seventy-five per cent. —were alive. These cases required on the average ten douches and a half; in half the number three douches and a half were sufficient.—*Lancet*, March 21, 1891.

THE THERAPEUTIC ACTION OF MONESIE BARK.

As is well known, monesie bark contains considerable quantities of saponine and tannic acid, and Dr. P. Rosanoff (*Journal de Médecine de Paris*, March 22, 1891) has made use of a watery extract of this substance as an expectorant and astringent in various diseases of the respiratory and alimentary tract, where its astringent properties serve to render it free from the disturbance of general digestion, which is so apt to follow the use of ipecac, senega, etc. In fact, it is even said to be useful in the treatment of chronic diarrhœa, and is especially indicated in chronic troubles of the respiratory organs where there is at the same time more or less digestive disturbance.

The Therapeutic Gazette

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Leading Articles.

NATURE AND TREATMENT OF DIPHTHERIA.

II.

PROBABLY no disease is the subject of more general interest to physicians than diphtheria, as none is a more favorite topic of discussion at medical meetings. Recent bacteriological researches, as detailed in the GAZETTE for March, 1891, have wonderfully advanced our knowledge of its etiology, while the therapeutics of diphtheria have hardly kept pace with this progress. The remedies proposed are legion, but all too poorly fulfil their end, and the mortality from this disease still remains very high. We are still without a specific, though the profession is looking for one; but physicians are learning more intelligently to combat diphtheria, and the gains which prophylaxis has made are great.

Under the head of the nature of diphtheria, there are two points to consider,—1, the question of its microbial region; 2, whether it is primarily a local or a general disease.

1. Till within a few years, nothing definite has been known about the contagion of diphtheria. There is now a growing disposition to accept as substantiated the claims alleged in behalf of the Klebs-Lœffler bacillus, especially in view of the recent confirmation of these claims by Roux and Yersin, of Paris, also of Drs. Abbot and Welch, of Baltimore. This bacillus is about as long as the tubercle bacillus, and about double the diameter of the latter; its extremities are rounded; it is immovable; it forms groups of chains, each element of which becomes club-shaped at its extremity. It is found exclusively in cases of diphtheria, in or beneath the false membranes; has been in vain sought in the blood and viscera. Culture experiments, made first by Lœffler in 1884, subsequently by Roux and Yersin, appear to have been successful; and with the product of pure cultures, the disease in all its essential features—not even the secondary paralysis in the experiments of the French bacteriologists being lacking—has been reproduced in animals. These experiments have been in part confirmed by Kolisko and Paltauf, of Russia, and by Drs. Welch and Abbot, of the Johns Hopkins Hospital; the latter have noted the invariable concomitance of the Klebs bacillus with the false membranes of true diphtheria. Other associated microbes, which doubtless have a *rôle* in the necrotic phenomena, have been observed in diphtheritic membranes, notably the *streptococcus diphtheriæ* of Prudden, which seems to be identical with the streptococcus erysipelatodes and the streptococcus pyogenes. Prudden, in fact, assigns to this micro-organism the principal part in the production of false membranes.

2. With regard to the second question, while there is not yet unanimity among the authorities, there seems to us to be *preponderant* evidence that diphtheria is primarily a local disease, the microbe (whether that of Klebs and Lœffler, or some other microbe) first causing a local inflammation, necrosis, and fibrinous exudation, then elaborating in the false membranes a peculiar poison,—a toxalbumén,—which is absorbed, infects and prostrates the organism.

It is true that there are difficulties attending this view in its application to all clinical cases; the gravity of the phenomena of infection is not always in proportion to the extent of the false membranes, and with an inconsiderable amount of local lesion the patient may from the first be overwhelmed by the

toxic accidents. Cadet de Gassicourt makes much of this argument, and classes such cases under the head of "diphtheria of hypertoxic form." On the other hand, it is equally true that there are benign cases where, with well-defined patches of false membrane covering considerable areas, the constitutional symptoms are trifling and almost *nil.*

There seems to be no better way to arrive at a true conception of diphtheria than by pathological experimentation, the results of which always bear out the view above stated *of a primarily local origin of the disease.* We have no space here for a statement of facts such as Oertel has given in his article on "Diphtheria," in the first volume of "Ziemssen's Cyclopædia," and which show conclusively that diphtheria, when induced in animals by the inoculation of bits of false membrane, is always at first local, fixing itself at the point of infection, *and thence radiating inwardly.* In harmony with this induction is the experience of Roux and Yersin with the soluble filtrates of diphtheritic cultures, which, injected in animals, produce septic accidents identical with the general constitutional effects of diphtheria in man. In accord with this doctrine, we may explain the grave, hypertoxic cases as cases of unusual susceptibility to the disease, where the poison, though coming from only a small centre, was rapidly absorbed, and met with but feeble resistance. In the *benign* cases alluded to, though the diphtheritic focus was of considerable extent, either the conditions for the elaboration and absorption of the poison were unfavorable, or the vital forces of the organism were peculiarly resistant to its influence; in fact, we are not without analogies which will enable us to understand such cases, in conformity with the view that diphtheria is primarily a local disease.

The treatment of diphtheria will naturally vary somewhat in accordance with views held as to its being primarily a local or a general disease. Those who believe in a primarily local origin will naturally have a strong interest in destroying *in situ* the morbid germs before they have had time to generate their virus and poison the organism. Under the other theory, the indication to promote local antisepsis and limit the spread of false membranes is equally recognized; but he who regards the diphtheritic *plaques* as only the expression of a general disease, bearing the relationship to the latter which the scarlatinal angina bears to scarlet fever, will not so strongly insist on energetic local treatment as he who looks upon the local lesion as the centre of the infection. Those, doubtless, that hold to the latter view have the most sanguine expectation that a specific will yet be discovered which, applied in time to the morbid focus, will nip the disease in the bud.

Certainly the results of the cauterization treatment, carried out with the intent of destroying the microbe *in situ*, have not been remarkably successful, unless we except the apparently favorable experience with carbolic acid and with phenicated camphor of Archambault and Gaucher, at the Hôpital des Enfants Malades; of Soulez, of Romorantin; of Sevestre, at Hôpital Trousseau; and of Dubousquet-Laborderie (vide *Bulletins et Mémoires de la Société de Médecine Pratique*, January 15, 1889). The method of these writers has been so highly vaunted that it deserves mention. The phenicated camphor is made as follows (we take the formula as given by Sevestre):*

℞ Camphor, 20 parts;
Castor oil, 15 parts;
Alcohol, 10 parts;
Crystallized phenic acid, 5 parts;
Tartaric acid, 1 parts.

Dissolve the phenic acid in the alcohol, add the camphor, then the tartaric acid, and finally the oil.

Gaucher applies this preparation in the following way:

"The mouth being widely opened and the tongue depressed, the operator will carry the swab charged with the liquid into the back part of the throat, applying it to the tonsils or other parts that are covered with false membrane. He will rub vigorously the diseased surface, in order to detach and remove the diphtheritic membrane, which will come away in *débris* or flakes. After each rubbing, the swab should be washed in a carbolic solution. These frictions should be repeated several times at each *séance* till all the white patches have been removed or destroyed. A final application with the swab dipped in the caustic will be made to the throat, in order to touch all the surfaces which have been denuded and despoiled."†

This operation is repeated morning and evening and in the interval of the cauterizations; large irrigation-injections are made every two hours into the throat by means of

* Sevestre, "Études de Clinique Infantile," 1890, p. 210.

† *Bull. et Mém. de la Soc. de Méd. Pratique*, January 15, 1889.

a fountain syringe of a 1 to 100 carbolic solution. The pain of the cauterizations is sometimes very great, but may be mitigated by previously spraying the throat with a cocaine solution.

Despite the fact that signal and unparalleled success is claimed for this treatment (see statistics of Gaucher, Legendre, Dubousquet), it will not be likely to come into favor on account of the painfulness of the cauterizations, the swelling which follows them (which necessarily hinders deglutition), and the difficulty, if not impossibility, of application in young children. Theoretically, this method is excellent; practically it demands for its execution a pitiless hardihood which few physicians possess. It is doubtful if in private practice the results would ever be even approximately as good as the French writers claim. The method of cauterizations is an old method, dating back to the times of Bonsergent, who cauterized the throats of young children with a red-hot iron, and Bretonneau, who did not even originate, but who borrowed from physicians of a past age a practice which consisted in swabbing out the diphtheritic throat three or four times a day with fuming hydrochloric acid. Trousseau, Rilliet and Barthez, and others adopted substantially this procedure, using muriatic acid, saturated solutions of nitrate of silver, sulphate of copper, etc., forcibly removing false membranes where they could, and cauterizing the denuded surfaces.

It is needless to say that the method of cauterizations, as formerly advocated by this school, has been deservedly pronounced a failure, and is now a thing of the past. Cauterization, as Cadet de Gassicourt says, does not prevent the patches from forming anew; it causes pain and dysphagia, and the more the derm is denuded, the more the extension of false membranes is increased and promoted.

It may, however, be said, in defence of the later method proposed by Gaucher and his colleagues, that it is less severe than the methods of Bretonneau and his school, as phenic acid is comparatively a mild caustic, and, in the diluted form in which it is used, effects little destruction of tissue, while being nocuous or destructive to the microbes. It may well be, as these writers claim, that, in cases of adults where this heroic treatment can be properly carried out, it may save life where other methods fail, due pains being always taken to keep the throat well disinfected in the intervals of the cauterizations by means of antiseptic sprays and irrigations. It is true that most authorities condemn all interference with the false membranes till they are separated from their attachments, and can be removed without violence to the parts beneath them.

Other aspects of the treatment of this disease will be taken up in another number of the GAZETTE.

THE TREATMENT OF ANÆMIA.

IN the treatment of anæmia, the *indicatio causalis* should be predominant. If the cause be hemorrhages, these should be stopped by internal and external styptics, by compression, by ice, ergot internally, etc. If profuse discharges (as prolonged suppuration) be the cause, such constitutional and local measures should be resorted to as will diminish or arrest them. Under this head come cold abscesses, bronchorrhœa, cystitis with copious muco-purulent exudation, chronic diarrhœa. Excessive lactation and excessive venery act in a similar way. While these inordinate wastes are going on, the blood is being spoiled of its richest elements,—its corpuscles and its plasmatic albuminates,—and any treatment to be efficacious must reduce to a minimum these losses.

If the cause be syphilis, tuberculosis, cancer, the causal indication is sufficiently plain. The victim of venereal disease may get rid of his anæmia and regain a fair measure of health and vigor under the reconstituent and antisyphilitic influence of mercury and potassium iodide; the tuberculous patient may improve by an out door life and a fortifying regimen generally; even the subject of cancer may be, for a time at least, benefited by medical or surgical means directed to his morbid condition.

The anæmia may be of toxic origin, being due to malaria, to poisoning by lead, by phosphorus, by mercury, etc., and the treatment will be addressed to such of these agencies as may be found to be operative in the particular case.

It would take up too much space here to enumerate all the causes of anæmia and follow out the indications. In idiopathic anæmia one of the most fruitful causes is insufficient food; then want of light and air, excessive bodily exercise, intense heat or cold, depressing emotions, are all important etiological agencies, and, when once recognized, will suggest the only successful means of cure.

Anæmia, moreover, besides being symptomatic of hemorrhages, profuse discharges, severe cachexiæ (as before mentioned), may arise from obstacles to taking food (as in stricture of the œsophagus), to dyspepsia, to organic disease of the heart, to chronic pulmonary disease, to fever, to dyspepsia, and, finally, to disease of the blood-making organs (lymphatic glands, spleen, marrow of bones). Anæmia originating in any of these ways can be successfully met only by attention to etiological therapeutics.

One of the most common forms of anæmia is that which is symptomatic of severe and prolonged dyspepsia, and for its removal demands a knowledge of the kind of dyspepsia,—whether atonic and functional, or the result of chronic catarrh, dilatation of the stomach, round ulcer, etc,—and the means, dietetic and remedial, to be employed for the restoration of the damaged digestive functions.

The anæmia of heart-disease is, of course, curable or incurable, according to the nature of the cardiac affection to which it belongs. Digitalis, strophanthus, nitro-glycerin, caffeine, adonidine, more than iron and arsenic, are indicated in this anæmia.

In the absence of any yet definitely known pathological lesions causative of chlorosis or of pernicious anæmia (although the theory which assigns both maladies to disease of the hæmatopoietic organs appears to be the most plausible), it is impossible as yet to fulfil the *indicatio causalis*, and we must content ourselves with attending to the *indicatio morbi*. In fact, in all kinds of anæmia this indication imposes itself upon the practitioner. To promote sanguification in all forms of anæmia, we rely on two orders of remedial agents,—medicinal and hygienic.

To take up, first, the medicinal means (though these are by no means the most important), there is still no medicine of such general utility as iron. It is true that we are still ignorant of the precise way in which iron does good, but the fact is none the less indisputable that in a multitude of cases under the influence of this agent the blood improves in corpuscular richness, and all the nutritive energies are augmented.

The ferruginous preparations are legion, and we believe, with Niemeyer, that special indications for the exhibition of one or the other of them cannot yet be laid down. In simple anæmia and in chlorosis almost any of the iron preparations are well tolerated, but in special cases it is necessary to select that kind which agrees best with the stomach. The citrate, tartrate, lactate, pyrophosphate, the reduced iron, Blaud's pill, the chloropeptonate are all mild preparations which are generally borne by weak and delicate stomachs. The tincture of the chloride (the most used of all the liquid preparations) sometimes acts with marvellous promptness and efficacy, but many patients cannot take it, and not every pharmaceutical product is reliable. Where iron alone does not agree, it may sometimes to advantage be associated with other medicines. Thus, the combination with aloes or aloin is especially valuable in many cases of anæmia or chlorosis with constipation. A favorite pill contains of dried sulphate of iron and extract of aloes of each one grain. To this is sometimes added for each pill one-quarter of a grain of nux vomica, a little capsicum, or one-thirtieth of a grain of arsenic. Dr. Julius Pollock urges the addition of a little rhubarb to the dose of iron in disordered states of the stomach. A combination which we have sometimes found efficacious is—

℞ Pulv. rhei, gr. ii;
Ferri carb. saccharat., gr. x;
Pulv. calumba, gr. v.
M. Ft. pulv. no. 1.

A pill much prescribed by Vulpian in anæmia and chlorosis (*Clinique Médicale*, p. 470) consisted of iron by hydrogen, soft extract of cinchona, pulverized rhei, of each equal parts; this was called the compound iron pill of Charité Hospital. The late Dr. Gueneau de Mussy (*Clinique Médicale*, t. i. p. 209), whose success as a practitioner is well known, was fond of a combination of bismuth with iron, and where the latter, despite the addition of bismuth, still produced irritation of the digestive organs, he did not hesitate to add a little opium or belladonna. This writer urges that it is not by furnishing to the blood an element that is wanting that iron does good, but by stimulating nutrition, and points to the fact that etiolated plants become green by watering them with ferruginous preparations, and at the same time their chlorophyll does not contain any iron.

Huguenin, of Paris, was one of the first to propose the hypodermic method of administering iron, especially in pernicious anæmia, where iron, when taken into the stomach, is not assimilated; and Dr. J. M. Da Costa, of Philadelphia, has used the dialyzed iron to advantage in this way. From 5 to 30 drops

daily may be injected under the skin without fear of abscess.

Arsenic has of late been highly extolled as a remedy in anæmia, especially in pernicious anæmia, and is said by excellent clinical authorities to merit a place next to iron; in fact, in many cases it does good where the martial preparations utterly fail. Drs. Byrom Bramwell, Mackenzie, Lockie, of England, have advocated the more free use of arsenical preparations for a tonic and hæmatinic effect. The latter, in the *British Medical Journal*, December 7, 1878, affirms that in many cases of anæmia approaching the so-called essential or pernicious anæmia, arsenic will confer more benefit than any other remedy. Dr. Wm. Osler, in the *Boston Medical and Surgical Journal* (vol. cxix. p. 454), reports remarkable results in puerperal anæmia from the continued administration of Fowler's solution, and reviews the history of the employment of arsenic in pernicious anæmia, and calls attention to the fact that we do not fully understand the reason why this drug should be so useful in some cases and so useless in others. It certainly has often the effect in profound anæmia much resembling that of a specific; like that of quinine in ague for instance. The initial dose should be 5 drops, gradually increased to 20 or 30 drops, three times a day. Puffiness of the eyelids, œdema above the eyebrows, vomiting or diarrhœa, indicate that the drug should be suspended for a time. The point of greatest importance is that this remedy should be given a long time and in increasing doses.

Other remedies, as phosphorus, manganese, cod-liver oil, malt preparations, alcohol, find their application in certain cases. Cod-liver oil is more readily oxidizable than any other fat, and when tolerated often constitutes a powerful auxiliary to other means of treatment. Alcohol, in the form of wine or ale, and sometimes where there is great debility, and especially in that anæmia which attends febrile diseases in the form of brandy or whiskey, frequently proves of aid in stimulating the functions of digestion and assimilation, and preventing inordinate waste.

But the hygienic treatment, which comprehends dietetics, exercise, hydrotherapy, aerotherapy, and climatotherapy, attention to rest, the restoration of normal habits of sleep, the rigorous avoidance of all excesses, of all injurious excitements, of depressing emotions, etc., is of far more importance than the medicinal treatment.

Hydrotherapy is a powerful stimulant of nutrition, and is commended by Fleury, Dujardin-Beaumetz, Becqueril, and others as one of the most active agents in the treatment of anæmia. The douches should be as cold as can be well borne, and should be very short at the commencement,—of not more than five or six seconds' duration.

The utility of out-door exercise, of sojourn in the country or at the sea-side, of mountain life, is sufficiently obvious as being among nature's best and most certain means of reinvigoration. Many cases of anæmia and chlorosis are due primarily to sedentary habits, to breathing hot or impure air, and to neglect of exercise. Without an entire change in the habits of living (due rest, sleep, and abandonment of every degrading, depressing passion being observed), the dietetic treatment of anæmia can do little good.

The dietetic treatment is, of course, the most essential, for it is only through the assimilation of food that we can hope for restoration. On this subject we must be very brief, as this article is already too long. As a general rule, food for the anæmic should be abundant, nutritious, and easily digestible. There should be predominance of albuminates (milk, eggs, meats, fish) over carbohydrates. Some patients will do better on light meals given frequently, others on not more than two meals a day. For patients with feeble digestive powers, beef peptones, underdone meats—even, for a time, pancreatized milk—may be necessary.

Some bad cases of anæmia and chlorosis do remarkably well on a dietetic system by stuffing, like that recommended by Dr. S. Weir Mitchell in his little treatise on "Fat and Blood." This is combined with much passive exercise by massage and electricity.

Gavage, or forced feeding, performed by the œsophageal tube, gives often brilliant results in certain anæmic conditions where it is impossible sufficiently to nourish the patient by mouth, but where food of a proper kind when introduced into the stomach is well digested and assimilated.

Some of the most discouraging cases are those that are attended with absolute repugnance to all food, as is often witnessed in pernicious anæmia. Medicines do little towards restoring appetite and digestion, and unless the physician can obtain hints from etiology and enforce the proper hygiene, he is powerless to benefit his patient.

THE ACTIVE PRINCIPLES OF PARSLEY.

IN modern as in ancient times parsley (*Petroselium sativum*) has enjoyed a certain reputation as a carminative, diuretic, aphrodisiac, and emmenagogue. Analyses by various investigators have shown that parsley contains a volatile oil, to which it mainly owes its odor and taste, and two indefinite substances, to which the name of apiin and apiol, the latter especially being supposed to be the active principle, have been given. Apiin appears to resemble pectic acid, while apiol is a yellowish oily liquid, not volatile, heavier than water, of peculiar odor, and acrid taste; is very inflammable, insoluble in hot or cold water, but very soluble in alcohol, in ether, and in chloroform. It has, however, been shown that the commercial apiol is merely the oleoresin. Although parsley has formed the basis of a number of chemical investigations, and several so-called active principles, in addition to those above mentioned, have been apparently isolated, no systematic study as to the physiological action of this plant has been published. Recently, however, Drs. Mourgues and Laborde have undertaken a series of experiments with a number of different products isolated from the parsley, and their results are published in *La Tribune Médicale*, Nos. 2, 3, and 4, 1891. Their experiments were made, in the first place, with a substance termed cariol, a new principle isolated by Dr. Mourgues from the parsley-seeds, but of whose chemical properties, however, no account was published; second, with a mixture of cariol and apiol; and, third, with crystallized apiol made by the process of Gerrichten. A comparison of the results reached with these different principles showed that the crystallized apiol is most poisonous, and yet at the same time absorbed with the greatest difficulty, and is consequently not available for therapeutic purposes. The apiolin of Chapoteaut seems to be the one which is most active, while at the same time being freest from disadvantages. This substance is prepared by exhaustion with light petroleum ether, the resulting liquid then being distilled, and the residue exhausted with alcohol. The alcoholic solution on evaporation gives a product which, on the addition of caustic soda, leaves a thick, reddish liquid, boiling at 275° C., with a specific gravity of 1113. This substance,—apiolin,—as determined by Laborde, in poisonous doses produces somnolence, stupor, paresis, and motor inco-ordination, with acceleration of respiration and pulsations of the heart, and finally death from asphyxia. In small doses its action is especially on the unstriped muscular fibre, leading to contraction of the vesical and intestinal walls, and especially of the uterine fibres; the latter is so marked in pregnant guinea-pigs as to almost invariably lead to the production of abortion. The authors group all the principles obtained from parsley, and all of which seem to have more or less activity, in the excito-motor group, since phenomena of exaggerated reflex excitability is one of the most constant results of its administration, which may reach such an extreme degree as to lead to the development of actual epileptic convulsions. They consequently attribute the action of the parsley derivatives on the muscles of the genito-urinary tract as being due to an overstimulation of the lumbar region of the spinal cord, and not directly to an action on the muscular fibre itself; while in poisonous cases the irritability extends to higher centres in the medulla oblongata, and then leads to the production of general convulsion, in the latter case not only the unstriped muscles but the voluntary muscles also being implicated.

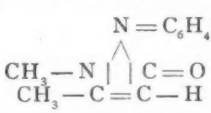
It seems, then, that there is some scientific reason for the generally-admitted value of parsley derivatives in dysmenorrhœa and amenorrhœa, and a series of cases, reported in the *Virginia Medical Monthly* for April, 1891, by Dr. Richard S. Hill (who employed the new prepration, apiolin, in capsules of 3 minims each, one being administered three times daily), seems to warrant the claims the author makes that apiolin is decidedly the most reliable drug which can be used in dysmenorrhœa. Only five cases are reported, but in these it is claimed that relief invariably resulted. It is unfortunate that as yet no reports of its use in amenorrhœa have been published, but if we are correct in assuming that we at last have a constant and reliable preparation of the active principle of parsley, we may expect improvement in such cases also.

IODANTIPYRIN AND IODANTIFEBRIN.

THE enthusiasm with which only a few years ago the search for antipyretics was prosecuted has now abated, for it was soon recognized that the morbid process in most cases was but little, or not at all, influenced by the reduction in body temperature. And yet the discovery of any new antipyretic must always attract more or less attention, for we

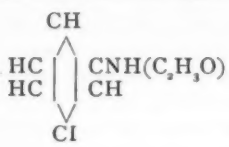
always have the hope before us in this way of discovering some specific remedy, to say nothing of the value of studies relating to the chemical constitution of such bodies and the influence of the nature of that constitution on the character of the results produced. Antipyrin and antifebrin are without doubt the two antipyretics which in the last few years have acquired the greatest reputation, while iodine as indisputably is a remedy which is one of the most valuable in our materia medica. The fact, therefore, that Dr. Ostermayer has succeeded in perfecting a chemical combination of iodine with both antipyrin and antifebrin would lead us to expect that such a compound might possess valuable therapeutic properties, and we, therefore, turn with interest to the report published in the *Prager Medicinische Wochenschrift* for January 28, 1891, and February 4, 1891, of a series of experiments made in this connection with these substances by Dr. Egmont Munzer in the clinic of Professor von Jaksch.

Iodantipyrin is antipyrin in which one hydrogen atom has been substituted by iodine; it is, therefore, iodphenyldimethylpyrazolon, $C_{11}H_{11}INO$, and its chemical constitution is in all probability the following:



It crystallizes in colorless, shining, prismatic needles; is with difficulty soluble in cold water and alcohol, more readily soluble in these menstrua when hot. It is absolutely tasteless, and has no especial odor. A two-tenths per cent. solution of this body does not prevent fermentation of grape-sugar. Its melting-point is 160° C. Dr. Munzer has studied the effects of this remedy in typhoid fever and in pulmonary tuberculosis, diseases whose temperature curves are well established. As regards the antipyretic effects of this compound, Dr. Munzer's results show that it corresponded absolutely with that of pure antipyrin, a fact which might be expected; for it is probable that through the action of the hydrochloric acid of the gastric juice this body would be decomposed, and we might, therefore, with reason look for the effects of antipyrin on the one side and iodine or iodide of sodium on the other. Dr. Munzer states that his results have shown him that in all probability such a decomposition actually does take place. He adds that, in doses of from 7½ to 22 grains, marked reduction of temperature is produced, which is accompanied by sweating, but without collapse and without chills. Pulse and respiration are slowed in proportion to the reduction of temperature, while the pulse becomes somewhat fuller and respiration somewhat freer. Eleven different cases are reported in which this substance was used as an antipyretic, the general result confirming the supposition above announced that its action is identical with that of antipyrin. The urine of every patient to whom iodantipyrin was given showed a marked iodine reaction after 15 to 22 grains of this remedy had been given, while the reaction of antipyrin in the urine with nitric acid was but faintly marked. If a perfectly clear, watery solution of iodantipyrin is tested for the iodine test with nitric acid and chloroform, a negative result is obtained, but a positive reaction is produced when either the solution or the nitric acid is heated, or when the reagents are allowed to remain in contact for half an hour. It would, therefore, seem that it is through the action of nitric or hydrochloric acid that the iodine of the iodantipyrin is set free, and the author reports some experiments which seem to show that this decomposition of iodantipyrin actually occurs in the stomach; so that, therefore, the therapeutic action of this remedy is not that of a new compound, but that which might be expected from the simultaneous administration of antipyrin and iodine, either free or in the form of a salt. It thus being seemingly established that this compound possesses no antipyretic effects other than those of antipyrin alone, the question naturally suggests itself as to whether the iodine when so administered in combination differs in its therapeutic effects from iodine administered alone. Here the author's experiments unfortunately are not sufficiently complete to admit of any conclusion. He, however, reports a case of persistent headache, apparently of syphilitic origin, which was rapidly cured by the administration of this compound, while a case of acute articular rheumatism is stated to have been entirely relieved from pain within six hours of the administration of the first dose. Further studies evidently are desirable before any positive conclusion can be formed as to the effects of the iodine in this composition.

Iodantifebrin is acetanilide in which a hydrogen atom has been substituted by iodine, the formula, therefore, being $C_6H_4INHC_2H_3O$, and its constitution in all probability the following:



Dr. Ostermayer prepared this substance from paraiodaniline, the product being with difficulty soluble in cold water, in alcohol, and ether, readily soluble in hot alcohol, and especially in hot glacial acetic acid. It has no taste and no odor, and melts at about 181½° C., and in two-tenths of one per cent. solution the substance does not prevent the fermentation of urine or of milk-sugar. The author's experiments as to the action of this substance show that, as an antipyretic, its effects were absolutely negative, and, in fact, no action was noted to follow its administration which could be attributed either to the antifebrin or to the iodine. This, of course, may be explicable as due either to non-absorption from its insolubility, or even, if it is absorbed, that the addition of iodine to its composition has destroyed the activity of the antifebrin. After its administration neither iodine nor antifebrin could be recognized in the urine, an observation which seems to show that this substance is not absorbed in the slightest degree by the alimentary canal; for tests of the iodantifebrin solution give both the iodine test and the characteristic antifebrin reactions. The author's experiments, therefore, are simply valuable as having removed two more substances from the list of new remedies from which wonders may be expected.

Reports on Therapeutic Progress.

ANGINA PECTORIS.

The meeting of the Medical Society of London, held February 9, 1891, was occupied by a discussion on the subject of "Angina Pectoris" (*British Medical Journal*, February 28, 1891). The discussion was opened by Dr. Douglas Powell, who urged that the subject should be considered on a broader basis, for angina pectoris was by no means so simple a malady as was supposed. The characteristic symptoms ranged between the wide limits of remediable functional disorder on the one hand, and fatal organic lesion of the cardio-vascular system on the other. He mentioned the case of a lady, aged 45, of neurotic temperament, who had complained of too forcible cardiac action for some years previously. There was a history of rheumatic fever fifteen years before, and five years ago, when riding hard across country, she was seized with severe cardiac pain and distress, and marked interference with respiration. These symptoms recurred on subsequent occasions. The pulse was small and cord-like, and of high tension. On using hard pressure, with one finger the pulse was felt almost, if not quite as well, as by a second finger placed further along the vessel, this phenomenon being evidently due to a back wave from the periphery. The heart's action was somewhat labored, intermitting twice in the minute; the first sound was muffled, but there was no distinct murmur. He regarded this as a case of angina of the first degree, or one of vaso-motor angina. He observed that one noticeable feature in this variety of the disease was the extreme restlessness of the patient, who often felt chilly and in need of exercise. In regard to this vaso-motor form of angina, he remarked that it was of comparatively recent discovery, and the prognosis in such cases must necessarily depend largely upon the actual condition of the heart. He regarded the vaso-motor disturbance as an essential factor in the majority of cases of angina pectoris, just as bronchial hyperæsthesia was in cases of asthma. He believed it to be possible for the heart to succumb to these attacks without itself being affected with any obvious lesion. He referred to the case of a medical man, aged 30, who consulted him on account of paroxysms of præcordial pain. On examination, there was no evidence of enlargement or disease of the heart, and he regarded it as an example of pure vaso-motor angina. A six months' rest from work left him apparently sound in all respects. He referred to another case in a gentleman, aged 68, in whom a marked improvement in the general condition occurred after an attack of gouty eczema. He remarked on the rarity of a fatal issue in these cases, the attacks if unrelieved by art usually coming to a natural end, probably through the action of the depressor nerve of the heart, and possibly some analogous mechanism of the small vessels under the stimulus of pressure inhibiting and controlling cardiac and vaso-motor spasm. He agreed with Dr. Broadbent's suggestion that some cases of fatal cramp while bathing were probably due to sudden oppression of heart from contraction of systemic arterioles; in fact, to vaso-motor an-

gina of an intense kind associated, perhaps, with a fatigued heart. Though physiologists maintained that when systemic arterioles were contracted by cold the visceral were dilated, and *vice versa*, yet it was highly probable that under certain conditions of chill and emotion the whole arterial system might undergo contraction. He quoted cases which seemed to show that the right side of the heart had borne the brunt of the anginal attack. The cardiac distress and rigid arteries of uræmia might, he said, almost be described as chronic persistent angina, though it was with the so-called cases of cardiac asthma in uræmia that the analogy with vaso-motor angina was most obvious. He then passed on to discuss angina pectoris gravior, in which the vaso-motor disturbance is associated with degenerative cardiac disease. He criticised the view that the disease was necessarily caused by or associated with disease of the coronary arteries. The prognosis in the first group was comparatively favorable, the probability being that death would ensue from some other cause, such as cerebral hemorrhage, while in the last group an almost certainly fatal result might be anticipated within a short period. Both for prognosis and treatment it was important to make out the precise condition of the heart in respect of size, position, and power. For the treatment of these two varieties, nitrite of amyl and nitro-glycerin were of great value, but far more so in the graver cardiac cases. In the first group they required to be associated with nervine tonics and sedatives, while in the second group carminatives and stimulants were of special value. He compared the pain in cases of sudden death from angina to that associated with embolic gangrene in the limbs. In conclusion, he described a syncopal variety of angina rarely met with, except in persons over 65, and then usually associated with gout. He suggested that undue acidity of the blood might be concerned in its causation. The attacks were often associated with dyspepsia, and the treatment indicated was careful feeding and gentle exercise. In conclusion, he said he regarded angina as a disturbed innervation of the heart and vessels associated with more or less intense cardiac distress and pain, and a general prostration of the forces, always producing anxiety, and often amounting to a sense of impending death. He grouped the varieties as angina pectoris vaso-motoria, angina pectoris gravior, primary cardiac angina, and syncopal angina; the first two forms bearing a remarkable resemblance to the respiratory analogue asthma.

Dr. W. M. Ord insisted on the remarkable parallel between the symptoms of asthma and angina pectoris. He pointed out that the term asthma formerly comprehended a great many varieties of difficulty of breathing, and statisticians had shown that in times past asthma was a very fatal disease, according to the returns, any reduction in this respect being probably due to better diagnosis. With regard, however, to angina, the condition was rather different; at present, people would have a larger range for angina than formerly, especially if they adopted Dr. Powell's conclusions. The old limited definition to which he alluded would certainly have to be extended to a large number of cases in which one or two only of the constituent typical symptoms of the disease, as first described, would be present. Such cases might, perhaps, be termed anginous, if not anginal. He pointed out that these anginous attacks usually came on in the daytime, and the prognosis was notably aggravated when they supervened at night. He compared the two classes of cases, one in which the patient had angina on exertion as the consequence of sudden arterial tension caused thereby, and the other in which the attack occurred independently of muscular exertion, and in these he thought the mechanism was probably nervous, either emotionally or by reflex. He had seen illustrations of both classes. He insisted on the importance of dyspepsia as a factor in bringing about the attacks, and observed that if he were restricted to one remedy in the treatment of angina he would prefer sulphate of magnesia to nitro-glycerin, in order to secure a regular action of the bowels. He mentioned the frequent coincidence of glycosuria with angina, which he thought authorized the inference that the visceral blood-vessels were dilated, and not contracted, as the author seemed to suppose, along with the superficial vessels. He said that the connection of gout with angina ought not to be forgotten, it being a neurosis, and involving, as it did, changes in the chemical constitution of the tissues. Treatment directed to the gout often relieved the angina. He insisted upon the fact that no sensations of an anginous type were to be treated lightly, and the patient or his friends ought always to be warned of the danger.

Dr. W. H. Broadbent said he had been unable to make up his mind as to the condition of the heart during the paroxysms.

Sometimes the pulse was irregular and small; sometimes there was high arterial tension, at other times not; while occasionally the pulse was practically unaffected throughout an attack even of great violence. The central fact, after all, in attacks of angina, was that the heart was overwrought, either by peripheral resistance or on account of intrinsic failure. That fact fitted in very well with the author's classification. It was especially in those cases due to weakness of the heart that the great danger lay. He pointed out that vaso-motor resistance alone would not be sufficient to determine an attack. The proportion of cases of high arterial tension without angina pectoris was very much greater than the proportion of fatal cases of angina in which there was no disease of the coronary arteries. He presumed that disease of the coronary arteries acted by causing degeneration of the cardiac muscular fibres. In bed and during sleep there was the upward pressure of the abdominal viscera and the curious running down of the cardiac powers to account for the supervention of the attacks. He pointed out that muscular exertion lowered very rapidly the resistance of the peripheral circulation. The effects of exercise were exerted principally on the right side of the heart. With reference to the neurotic theory, he pointed out that the vast majority of anginal cases occurred in the non-neurotic sex, being extremely rare in women. They ought, therefore, to beware of attaching too much importance to an unexplained neurosis. The occurrence of angina in gouty people he ascribed to its association with high arterial tension. He had also noted the existence of a myocarditis in patients suffering from glycosuria, associated with high arterial tension, and this was usually followed by marked anginal paroxysms. He remarked on the fact that angina was seldom or never associated with mitral lesions, and anginal symptoms usually subsided on the supervention of a mitral lesion in a person subject to anginal attacks. His own experience seemed to show that the gravest cases of angina were those in which the least explanation could be found to account for the symptoms.

At the meeting of the London Medical Society, held February 23, SIR WALTER FOSTER, of Birmingham, reopened the discussion on "Angina Pectoris" (*Lancet*, February 28, 1891). He agreed with Dr. Powell that a broad basis should be taken for consideration of this subject, for under this title could be grouped a series of conditions, from trivial remediable disorder to severe attacks of terrible heart-pangs, ending in sudden death, and, if they were considered as a whole, some ideas might be built up as to their pathology and treatment. He first desired to refer briefly to four cases. The first was that of a doctor, aged 64, who complained of angina pectoris, which came on in the course of the night. The symptoms were described as those of intense pain, which developed in the region of the nipples and radiated down the left arm, and he was seized with terror and a sense of impending dissolution. Under sinapisms and free stimulation he was relieved. It was in this patient the beginning of a gouty condition, and attacks were afterwards induced by walking up-hill. The patient died of a dilated heart eight years afterwards. He saw another case in the year 1863, when he was in charge of a friend's practice in the south of London. It was that of a young man who was a good runner, and who one evening ran the length of the street for a wager. When near the end of the street he uttered a sudden cry and died in a few minutes. A careful necropsy revealed the left cavities empty, the right ventricle almost so, while the right auricle was enormously distended. In his death-agony he complained of intense cutting pain in the chest. In another case, a prematurely old man, aged about 56, complained of intense pain across the chest; the pulse was slow, not more than 50 to the minute, and was of high tension. During the attacks the pulse fell to 36, and became intermittent; there was pain between the nipples, down one or both arms, together with much anxiety, general clammy sweats, and pallor of the face. Against advice he married a young wife, and though he survived very well the earlier weeks of matrimony, he died eleven months later, and at the necropsy no valve lesion was found, and there was no aortic atheroma. In another case, which occurred in a medical man, he graphically described the attack. The pulse fell to 20 at the wrist, though the heart was beating more frequently, and it was small, irregular, and hard; the face was pale, there was no pain in the chest, but he felt that he was dying. Sinapisms were applied to the chest and hot bottles to the feet, while strophanthus, with ether and ammonia, were given internally. Under this treatment he recovered; he put it down to a neurotic attack induced by influenza, and influencing the pneumogastric nerve. Later he had a second attack, slighter in degree, but

he died in the midst of a third, which came on at night, and was associated with well-marked heart-pang. No necropsy was made, but there was no indication during life of organic disease of the heart or arteries. These cases illustrated certain features of the affection, and he wanted to compare them with other cases,—cases in which there was agonizing pain accompanied by grave organic disease. In one man, who committed suicide on account of the anguish, there was double aortic valve mischief, with an aneurism springing from one of the sinuses of Valsalva, and pressing on the root of the aorta and on the cardiac nerves. In the cases of valve disease which suffered the most pain there was considerable dilatation of the left ventricle of the heart, with, later, degeneration of the cardiac muscle. As this dilatation was usually associated with aortic disease, it confirmed Dr. Walshe's remark that the cases of disease of the basal valves were those associated with angina. He had once witnessed a case of rapidly-developing insufficiency of the aortic valves produced by a sudden strain. The patient had severe chest pang, and was collapsed and insensible. He was bled from the arm and rallied, and was then found to have aortic regurgitation, although he was known before the strain to have sound valves. For days he complained of stretching pain under the sternum, due to dilatation of the ventricle. The same kind of stretching pain was met with when further dilatation was in progress in an already diseased heart, as when the hypertrophied muscle underwent degeneration late in Bright's disease; and such cases were relieved by the establishment of mitral regurgitation. In all these cases he had related he believed the immediate cause of the heart-pang to be distention of the cavities of the heart, either right or left. In the case of the patient who got his attacks when walking up-hill, the right was involved, while in the gouty patient, in whom the attack came on at night, it was the left ventricle which could not overcome an increased vascular pressure, brought about, perhaps, by the circulation in the blood of some excess of uric acid. He held that stretching and not spasm was meant by the "distentio" of Heberden. He thought that in all or nearly all the cases there was a degeneration of the myocardium, with distention of the cardiac cavities. This view was counter to that of neurosis, but he knew of no direct evidence to support the idea of spasm of the coronary arteries. In Sir Richard Quain's revised article on "Angina" he referred to Dr. McWilliams's recent researches as to the nature of "delirium cordis" in animals in which there was a quick irregular cardiac action, with fall of blood-pressure due to a distended ventricle remaining in a state of diastole and excited by trivial causes, such as distention of the gut. He preferred to regard angina not as a disease, but as a mode of death and a term under which might be grouped a number of allied conditions having a common pathological basis. In the treatment a scientific step had been made when drugs like nitrite of amyl and nitro-glycerin were introduced, which counteracted the vascular condition which was the starting-point of the malady. If the pain were prolonged, morphine subcutaneously was indicated, while in the intervals no drug was more valuable than arsenic, with ether, iron, bromides, or alone. Iodide of potassium, in doses of 5, 10, or 15 grains three times a day, had wonderful power of lessening the pain and improving the patient's condition. The female sex were not troubled with angina because they were less exposed to strain of the heart than men.

Professor Grainger Stewart, of Edinburgh, found that his line of thought diverged considerably from that of the previous speaker, and he referred to the interesting comparisons that had been made between glycosuria and asthma and the affection under discussion. Cases of angina grouped themselves into four categories: 1. Simple neuralgia of the heart, seen in women at the climacteric, and in men of gouty constitution, in which pain was referred to the heart itself, and was very amenable to treatment. 2. A condition of angina dependent upon and associated with acute or subacute inflammation of the aorta. He had more than once seen a patient describe a curve on his chest, like that of the aorta, to indicate the site of his pain, and he described a case in which pain was referred to the lower part of the thoracic aorta which recurred in paroxysms and travelled gradually higher up. Later a marked double aortic murmur developed, and death occurred. There was no post-mortem, but aneurism, pleurisy, and new growth had been excluded, and he considered that the case had been one in which an aortitis had commenced low down and had spread upward, damaging the valves and producing dilatation of the heart. Though this latter had only developed at the last, pain had been present from the first, and had been of true anginous character. 3. A common group of cases in which angina pectoris was associated

with fatty, fibrous, or other degeneration of the cardiac walls, or with changes in the coronary arteries. 4. Angina pectoris associated with spasm of the arteries and increased tension. There was very little change in the heart, but it was overmastered by the arterial spasm without the coronaries or substance of the heart being necessarily involved. As to the determining causes of anginal attacks, many of them would apply to all four groups. They were exertion, emotional excitement, such as anger or grief, dyspepsia, constipation, the various toxines absorbed into the system from the intestines, or from failure of the kidneys or other eliminants, and certain changes in the nervous system, such as, for instance, occurred when sleep was setting in; each or all might suffice to bring on an attack. But in any of the last three pathological groups the same lesions might exist without pain; so that one had to ask one's self what was the explanation of the pain when it occurred. Was it of muscular or of nervous origin? Sir Walter Foster had said that it was a muscular pain, but he did not know what spasm of the heart-muscle meant; he doubted very much if it were like cramp, though a vague idea to that effect still floated in the minds of some. What seemed against this was that the heart and pulse might remain steady all through an attack, and if aortitis could of itself be a cause of angina, that vessel did not contain enough muscle to produce a painful cramp. He therefore looked upon it as a pain of nervous rather than of muscular origin. Inquiring whether any purely nervous diseases resembled angina, he pointed out that epileptiform neuralgia was wonderfully like it, coming on in sudden paroxysms, and often ceasing as suddenly, leaving the patient well, but subject to a new attack, being more common in men, and at or after the middle period of life. Certain slight peripheral influences would provoke intense pain, which was relieved by cutting or stretching the affected nerve. So also in angina, explosions of pain occurred from time to time in connection with irritation in the aorta or heart, the cardiac nerves being capable of afferent as well as efferent function. In short, he suggested the essence of the process to be a change of organic or functional nature in the nerves or nerve-endings which controlled the heart, and he added that distention of the heart did not necessarily produce pain. For treatment, he agreed that the general health should be improved, excitement and effort being avoided, and nitrite of amyl administered to relieve spasm. The latter drug he believed had also a direct effect on nervous structures, for it relieved other neuralgiæ. Arsenic and iodide of potassium were invaluable, and occasionally direct cardiac tonics, such as digitalis and strophanthus, might be given with benefit.

Professor MacVail, of Glasgow, agreed that the basis of the whole subject should be broadened, so that any condition of pain about the heart should be alluded to as angina. As regarded the pain, it might be general or partial. He had seen two cases in which it was likened to a knife plunged into the apex of the heart; in another it was as if needles had been driven in; in another as if crushed or grasped; and in yet another as if greatly dilated, the patient actually feeling to ascertain if his chest was not bulged out. In some the pain was radiating, in others it was distinctly local. The question of radiation depended on two circumstances,—on the amount of the pain and on the ability of the nerves to conduct. People differed from one another, and the same people differed at different times with regard to their power of conductivity. In one of the cases above mentioned, in which the pain was knife-like, there was no radiation; but in the second case of knife-like pain it passed from the cardiac apex to the left shoulder. In the case in which the pain was like needles it passed from the apex of the heart to the scapular angle, thence to the top of the left shoulder and down to the bend of the arm. In the case in which the heart felt to be dilating, the patient either became faint or was confused mentally; this might be due either to an insufficient blood-supply to the brain, or it might be really an instance of radiation, and thus resemble some of the mild forms of epilepsy. Not only did pain radiate from the cardiac seat, but before the attack began a sensation might also travel towards the cardiac area. It was a kind of aura. In one case, that with the crushing sensation, the patient described a sensation of burning or of boiling water poured on a small area of skin near the umbilicus; thence it travelled towards the heart, and then the attack of angina commenced. In the case where the pain was like needles, it commenced at the inner end of the left seventh interspace; thence it travelled to the apex of the heart, which took five minutes; from there the pain went to an inch below the scapular angle, taking ten minutes, and it was now no longer like needles, but like a knife; thence to the left

shoulder in five minutes, and finally to the bend of the arm in two minutes. The connection between angina and epilepsy was worth more attention than had been paid to it, and in every case an antecedent sensory condition should be inquired for. He had found the organic conditions present to vary much; in one of the cases of knife-like pain there was a double mitral murmur, while in the other there was mitral regurgitation alone. In the instance where the sensation was of a crushing character there was a double mitral murmur; in that in which a sense of dilatation was complained of, the condition was one of double aortic trouble. In the case where the pain was like needles, no organic abnormity could be made out. What was the actual condition of the heart when the pain was present? Sir Walter Foster and Professor Stewart had contended that it was not cramp. Was it possible to separate cramp from a neurotic condition? Though it might be done in laboratory work, it was quite impossible to separate them in practice. He himself was quite unable to separate the nerve condition from the muscular condition of the heart as regarded pain. An ordinary muscular contraction was a pleasurable sensation, as in exercise; but if the contraction were much increased in intensity, as under strong faradism, it then became painful, and was a condition of cramp. The muscular condition in the living body was always one of tonus; there was no such thing as complete relaxation during life. It had long been taught that the cardiac contraction was not one of physiological tetanus, but this idea had been proved beyond all dispute to be false. If over-contraction were present, it was simply a question of degree whether pain would be present or not. Dr. Walshe had objected to angina being due to spasm, because he held that, if it were due to spasm, the heart would necessarily remain continuously contracted during the spasm. But this by no means followed, for if the upper extremities were thrown into a condition of tetanus by means of the faradic current, it would be still found possible to move the hands, unless, indeed, the current were extremely strong; so in moderate cases of angina the tetanic spasm was not strong enough to interfere with the impulse. Dr. Walshe likewise stated that as in diastole the ventricle was flaccid, the angina, if due to spasm, should be intermittent. But there was no evidence to show that the ventricular wall ever became flaccid even in diastole. The presence of a murmur in aortic regurgitation was fatal to the idea of the ventricle ever giving up its grip of the blood. The idea of this murmur being caused by valve vibration was of course absurd, and Balfour had shown that it was caused by a thin stream of regurgitant blood forcing its way back into a mass of blood remaining in the ventricle under considerable tension. If the ventricle were thus never quite flaccid even in diastole, it removed the great objection to the theory of spasm. He thus upheld the old idea of Heberden, as supported by Latham, that the condition of angina was immediately dependent upon spasm of the heart. The excessive irritability of nerve and muscle caused by overwork induced instability of the nerve-centres, and if the explosions from the unstable centres became sufficiently frequent, then a condition of cramp would result. He asked, in conclusion, that each individual case should be examined in reference to the order in which the parts were attacked by pain and the directions into which it radiated.

The meeting of the Medical Society of London, held March 9, 1891, was also devoted to the continuation of the discussion on "Angina Pectoris."

At this meeting, Dr. Lauder Brunton, in reopening the discussion, observed (*British Medical Journal*, March 14, 1891) that in discussing the subject much help might be obtained from the analogy pointed out by Professor Grainger Stewart between the heart and the bladder. Both were hollow muscular organs, contracting and dilating at fairly regular intervals, and expelling liquid contents. In both slight distention formed a stimulus to contraction; but, if the distention became excessive, it might cause pain, varying in amount from slight discomfort to extreme agony. The sensation of pain, he said, was always central, for it depended on a condition of the brain which might be excited by a peripheral irritation like a diseased joint, but might exist quite apart from any peripheral disease, as in hysteria. A mixed condition might exist which was both central and peripheral, as in the vesical arises of locomotor ataxy, and possibly a similar condition might occur in the heart. Usually distention, either of the bladder or the heart, not only caused contraction in them, but, through the nervous system, lessened the resistance of the sphincter in the case of the bladder, or of the arterioles in the case of the heart. Disturbance of this nervous relationship might cause excessive distention

or pain in either organ apart from organic disease, giving rise to spasmodic retention of vaso-motor angina. But while the spasmodic character of angina pectoris indicated its nervous origin, it was so frequently associated with diseased coronary arteries and fatty heart, that these evidently played a great part in its causation. Angina pectoris might be said to be due neither to high tension alone, nor to weak heart alone, but to weakness of the heart in relation to the resistance it had to overcome; and it might be brought on either by weakening the heart or increasing the resistance, or both together. In tracing out its pathology, the analogy with the bladder was useful. The resistance which the heart had to overcome depended upon the contraction of the systemic arterioles. Of these there were three subdivisions,—cutaneous, visceral, and muscular,—and the latter was the most important in relation to the attacks of angina. One of the most striking symptoms of angina was the ease with which it was brought on by muscular action. The first effect of this was to prevent the passage of blood through the muscles and to raise the tension, although afterwards the vessels of the muscles dilated and the tension fell. To this primary rise Dr. Brunton attributed the occurrence of anginal attacks on exertion; and their passage off, if exertion could be continued, was, he considered, due to the subsequent dilatation of the vessels of the muscles, with consequent fall of blood-pressure and lessened resistance. He thought that atheroma of the coronary arteries was so powerful in causing angina because it prevented the supply of blood to the heart being increased on exertion, as it ought to be in muscles generally. The pain of angina he considered to be due to distention of the heart, and its more common occurrence in the left than the right side of the heart to be due to the greater ease with which the tricuspid valves became incompetent than the mitral when the ventricles became dilated. Angina pectoris was very rare in children, but one case was recorded of a boy, aged 14, in which there was aortic regurgitation and mitral stenosis; and another in a boy, aged 11, where there was ossification of the auriculo-ventricular groove, conditions which would prevent dilatation of the mitral orifice and insufficiency of the valves. He agreed with the previous speakers in regard to the necessity for the elimination of waste products, and also for restricted diet in gout, and for the use of iron and arsenic in feeble heart; but he regarded the nitrites as the most efficient remedy during a paroxysm, and, on the whole, iodide of potassium as the most useful in the interval. He showed a tracing which appeared to indicate that it lessened the rise of blood-pressure in exertion, and mentioned a case illustrative of its remedial action.

Dr. J. Mitchell Bruce said he should confine his remarks to a few practical points, the first being what was called vaso-motor angina. He had seen a great many cases answering to the description that had been given of this vaso-motor angina, but he did not think that they were really cases of this kind; indeed, he was of opinion that such cases were very rare, and the term as generally employed was not only unfortunate but misleading. He pointed out that in most instances the malady occurred in elderly people, between 40 and 50, inclined to be stout, and who had led an anxious but not overactive life,—men who had achieved an independence and felt entitled to enjoy themselves a little. They sooner or later had symptoms of irregular gout, and he insisted upon the fact that such patients were unlikely to present a hard pulse, for they were generally weak and nervous. Moreover, there was very frequently a history of cardiac strain, and the first attack of angina was often referred to a particular instance of overexertion. When men with this gouty disposition strained their heart there was a tendency for the gout to attack the heart, just as it tended to attack other parts of the body that had been subjected to strain. If an attack of acute gout supervened, it might be associated with a rise in the blood-pressure, but its effect was not to make the patient worse, but to relieve him. They were thus confronted with the observed fact that an attack of angina was relieved by a condition which might be expected *a priori* to aggravate it or to bring it about. He maintained, therefore, that high tension was not a usual factor in the production of angina pectoris. In the matter of treatment, he recommended muscular exercise, attention to diet, iodide of potassium, and the use of purgatives. He suggested that the use of the term "vaso-motor angina pectoris" should be abandoned in favor of some such description as "gouty heart," which described a pathological condition, and not a mere collection of symptoms. With regard to the classical angina, he had been struck by the large proportion of minor cases as compared to the severe ones. He remarked incidentally upon the involuntary passage of a copious

motion at the onset of a severe attack, and he concluded by expressing surprise that nothing should have been said in reference to the so-called pseudo-angina.

DR. F. DE HAVILLAND HALL observed that gout of the heart was a not uncommon cause of death. The condition described as "gout of the stomach" was often due to angina, the cause in other cases being gall-stone colic. He mentioned that angina pectoris and gall-stone colic were often confounded, relating a case in support of this view in his own practice. He alluded to the effect of cold in precipitating the attack of angina in certain patients, and mentioned that these were precisely the cases in which nitroglycerin did the most good.

DR. SEYMOUR TAYLOR said he had made a special study of heart spasm, and divided cases of angina into cardio-vascular, neurotic, and reflex. He called attention to the fact that angina was mostly met with in patients belonging to the better classes.

DR. FLETCHER LITTLE related three cases illustrating various clinical features of the malady.

DR. J. ROSS (Manchester), who was not able to be present, had written a letter to suggest a theory to account for the distribution of pain in angina. His idea was that the local pain was conducted to the portion of the spinal cord corresponding to that from which the diseased viscus derived its splanchnic nerves, and then spread through the posterior horns of the gray matter, and led to eccentric projections referred to the terminations of the somatic nerves derived from the same segment of the cord.

PROFESSOR GAIRDNER, of Glasgow, also wrote, expressing his inability to recognize the angina pectoris vaso-motoria of Nothnagel as a true clinical description, and he thought that the term was positively misleading. He admitted that there might be a vaso-motor element in Heberden's angina, but urged that this was distinctly subordinated to organic structural changes in the heart.

The PRESIDENT, in reply, said he was unable to divest himself of the view that the cause of the pain was spasm of the heart resulting in distention, and he could not rally to the idea of its being due to neuralgia. He pointed out that neurotic affections were invariably associated with disturbance of function, and yet it was a matter of observation that in certain cases of angina the action of the heart was not interfered with even during the attacks. This militated strongly against the neuralgic theory. He dissented from the view that angina was not usually associated with lesions of the mitral orifice, and observed that this was at any rate not his own experience. Moreover, it was generally at the mitral orifice that evidence of degenerative changes were first met with in elderly and gouty people. With reference to the relative value of nitrite of amyl and nitroglycerin, he usually gave preference to the former. He mentioned a case in which the dose had been carried to 7 minims three times a day, rising to 35 drops during an attack, the dose being repeated after a short interval. Special attention had been paid to insure the solution being of the proper strength. He observed, however, that such doses could only be safely resorted to with the patient under close observation, and very gradually. With regard to the exercise treatment, he said he would be very sorry to advise it in what he still regarded as a definite class of cases,—namely, the vaso-motor anginas. In these cases muscular exercise would be likely to prove injurious. He concluded with an expression of gratitude to those gentlemen who had joined in the discussion, regretting that time did not permit of a fuller reply to their very interesting remarks.

SOME COMPLICATIONS OF CHLOROSIS.

The manifestations of chlorosis may occur in the most varied forms, and in certain complications they are a source of great danger, seriously interfere with a favorable prognosis, and cause difficulty in the diagnosis. Two of these especially deserve attention,—thrombosis and fever. These two complications have been made the subject of an essay in the *Revue de Thérapeutique Medico-Chirurgicale* for February 1, 1891, by DR. SICARD, who calls attention to the fact that thrombosis in the course of chlorosis nearly always occurs in the form of phlegmatia alba dolens, which is a rare complication, it must be admitted, though numerous cases have been reported in the last few years.

Trousseau, many years ago, was the first to recognize its existence, and stated that undoubtedly the reports of the frequency of the complication would be much greater if attention was directed to the possibility of its occurrence. Thrombosis may occur in any period of chlorosis, but it especially occurs when the disease is severe and undergoing rapid progress, although it may also occur in cases of moderate severity, and ordinarily makes its appearance

at the commencement of the affection, when the cachetic condition has not yet been developed. This complication may appear spontaneously, but fatigue should be considered as a predisposing cause. The lower extremities, and especially the left leg, is ordinarily the seat of a venous thrombosis. It has, however, been recognized as occurring in the vessels of the upper extremities, and sometimes even in the cephalic blood-vessels, but in the latter condition the thrombosis may even occur in the arteries, especially the artery of Sylvius, or sometimes in the venous sinuses. Perhaps in this latter case the immediate causes of thrombosis have not always been eliminated, such as severe affections of the middle ear or infectious tonsillitis.

A case reported by Charmeil proves the reality of thrombosis of the sinus due to chlorosis. The case was that of a young woman, 24 years of age, free from any syphilitic, tubercular, or rheumatic affection, in whom severe cerebral symptoms developed after exposure to the sun. There was violent headache, insomnia, disturbance in the co-ordination of the pupils, delirium, and death resulting in coma. The autopsy demonstrated cerebral softening, due to a thrombosis of the superior longitudinal sinus. Vergely, also, has related two cases of arterial thrombosis occurring in chlorotic cases in whom at the autopsy the left Sylvian artery was found obliterated by a clot. In addition to the state of the blood, which predisposes to coagulation, the condition of the circulation in the Sylvian artery favors the production of this accident.

Finally, Rendu has reported an observation of spontaneous thrombosis occurring in the pulmonary artery during the course of chlorosis. With the exception of these very rare cases, thrombosis in chlorotic patients nearly always occurs in the veins of the lower extremities, usually on the left side, and so is a true phlegmatia alba dolens, whose anatomical location may be attributed to the readiness with which circulation in the left iliac vein may be compressed by distention of the sigmoid flexure. Consequently, it occurs usually in patients subject to constipation.

The phlegmatia of chlorotic patients usually appears suddenly, pain of moderate intensity occurs in the calf of the leg, and radiates through the leg, either downward or towards the thigh. At the outset, walking is not interfered with, and the accustomed occupation is not necessarily stopped; however, by the end of two or three days, the intensity of the pain becomes such that the patients are forced to remain in bed. It may be noted that the œdema is the first symptom to call attention to the disease, and this may occur either in the upper part of the thigh or in the calf; but it is always very rapid, more so than in the phlegmatia of other causes.

The beginning of thrombosis is also indicated by fever, which, in some cases, precedes by one or two days the appearance of the complication or even the first signs of pain. The temperature, more elevated in the evening than in the morning, may pass 104° F., but the thermic curve possesses no special characteristics. The febrile excess is proportionate to the extent of the local lesion and the degree of lymphangitis, or to the presence of other complications, which should be always looked for. The aspect of the limb is similar to that observed in cases of phlegmatia: there is white œdema, with extensive infiltration of the part, while red and painful streaks denote the inflammation of the cutaneous lymphatics. Palpation causes acute pain over the course of the affected veins, and should the pain not be very severe, the veins may be recognized under the fingers in the form of solid cords. Exploration, however, should be performed with the greatest care, and should not be prolonged, as it is by no means free from danger.

Phlegmatia occurring during the course of chlorosis is usually of slow progress, its duration varying from twenty days to two months. Of course an embolus may be detached and carried to different parts of the system. The symptoms due to pulmonary emboli vary with the size of the clot, though cases are on record in which sudden death occurred from suffocation. This possibility should always be borne in mind by the physician, but with this reservation, it may be stated, that the prognosis in chlorotic thrombosis is usually a favorable one. The diagnosis of the condition itself is not difficult, but it is a point in which careful attention should be directed, for the cause should not be attributed to chlorosis but by exclusion, consequently careful examination should be made as to whether there exists any cachexia, any general dyscrasia, or any infectious disease. In the female puerperal complications should be looked for, or a possible lesion of the genital organs. As to the mode of production of thrombosis, two conditions may be concerned, the one relating to the state of the blood, the other to the walls of the blood-vessels. The alterations of the blood are by no means doubtful in the course of chlorosis, and the experiments of Hayem on intravascular injections seem to establish that an-

æmia facilitates the production of concretions. It may be that the blood by its alterations contains in itself the cause of the coagulation. It is interesting to determine what leads to the production of the thrombosis at any one point rather than at another. This is to be explained as due to the induction of vascular lesions. The extreme anæmia may lead to fatty degeneration of the internal walls of the blood-vessels, but this lesion can hardly explain the production of thrombosis at the onset of chlorosis, or where the disease has not made very marked advances. Rendu attributed to micro-organisms the principal *rôle* in the phenomena of coagulation in thrombosis, for the chlorosis, according to him, acting as a debilitating disease, depresses the organism, and so favors the invasion of germs. It must be admitted, however, that the genesis of chlorotic phlegmatia is far more from being clearly elucidated. The treatment of the complication does not differ from that which would be applied under other circumstances. It consists principally in the most complete repose, the patient being warned against moving, lest the motion might lead to the detachment of a part of the clot. Constipation should be combated with enemata, for the accumulation of fæces in the sigmoid flexure by disturbing circulation interferes with resolution. The pain may be combated by application of the extract of belladonna, while if the fever is at all marked, recourse should be had to quinine.

The second complication, which is not rare in chlorosis, is fever, to which Dr. Molière was the first to call attention. This author has shown that in nearly all cases in chlorotics the mean temperature of the body is above the normal, and is usually about 100½° F. The type of the fever in chlorosis is not, however, always the same. In most cases the temperature-curve is characterized by very slight oscillations, which do not extend over 1°, and the fever is, therefore, a slight continued fever. In rare cases, the fever may develop exacerbations, in which the temperature will rise to 104°, and Dr. Potain has reported the case of a young chlorotic girl with a constant temperature of 103°. In spite of the uneasiness which this state might occasion, the fever disappeared completely when cure of the chlorosis was produced. Fever does not occur in chlorosis until the anæmia has reached a very advanced stage; but, of course, before attributing the fever to chlorosis, careful examination must be made to eliminate all other possible causes, such as gastric disturbance, angina, or other disturbances which might cause the attack. Sometimes, also, it should be recollected that the fever occurs under the influence of fatigue or prolonged exercise. According to Dr. Hayem, fever does not occur in chlorosis until the globular richness of the blood expressed in healthy corpuscles is below one and one-half millions, although sometimes there is no proportion between the fever temperature and the anæmia; but it has been demonstrated that complication is, in the majority of cases, closely associated with the chlorosis, for in those cases where its appearance has been noted and other causes excluded, it disappeared under remedies which cured the chlorosis. It is difficult to explain the production of fever, which is to be regarded as a sign of exaggerated oxidation in chlorotic individuals, where all the nutritive operations are depressed far below normal. The most reasonable explanation is to attribute it to some heat-regulating mechanisms of the body by which the balance between heat production and heat dissipation is interfered with. Of course vaso motor phenomena are likewise maintained, and there may be chilling of certain peripheral processes, and increased temperature of others, while urea always is increased during the causation of fever.

The principal interest in the study of fever in chlorotic cases is found in the difficulty which it adds to the formation of a diagnosis. The first point to establish when one meets with the presence of fever in a chlorotic individual is to endeavor to determine the cause of the fever. A careful examination should, therefore, be made of all organs, looking for a possible cause of infection. The urine should be examined, and if the amount of urea is that which is usually found in chlorosis, one would be authorized to believe in the existence of the febrile form of the disease. Especially should care be exerted in looking for a possible latent tuberculosis. Emaciation is one of the earliest signs of this, and every young pale girl, who at the same time loses weight, should be placed under careful observation and watched with the greatest solicitude. Cough and the phenomena developed by auscultation are of less value, for the cough exists in chlorotics, and the stethoscopic signs are often very obscure in many cases of tuberculosis. In tuberculosis, however, a temperature is ordinarily met with which is unknown in chlorosis, and if the temperature is above 104° or 105½°, if the pulse is maintained at 120 to 130, the situation should be regarded as grave and a rapid tubercular affection suspected. Of course these remarks only apply to cases in which signs of auscultation or the detection of the bacilli

have not made the diagnosis positive. The fever occurring in chlorotic patients does not call for any special indication as regards treatment. It is combated by the treatment intended to combat the anæmia,—that is to say, by well selected iron preparations and suitable regimen. Dr. Hayem has, however, called attention to the advantage derived from the use of cold applications, and in all cases of intense chlorosis where there is a tendency to syncope or the patients are easily exhausted, the wrapping in wet sheets is of the greatest efficaciousness. A revulsive effect is obtained, and at the same time a stimulating and a nervous action. Once or twice daily the patient should be wrapped in a wet sheet, and the application continued for two or three minutes. In all cases, however, the fever is not to be regarded as constituting any special source of danger. It deserves, however, attention mainly from the fact that its occurrence is always associated with chlorosis of very intense form.

ULCERATIVE ENDOCARDITIS.

At the meeting of the Metropolitan Counties Branch of the British Medical Association, held February 4, 1891, Dr. Frederick Taylor read a paper on "Ulcerative Endocarditis," in which he defined the disease as a febrile process, resulting from recent, often ulcerative, lesions of the endocardium, accompanied, as a rule, by evidences of embolic obstruction in different parts of the body (*British Medical Journal*, March 7, 1891). He recorded a case, recently under his care and that of his colleagues at Guy's Hospital, in which the characteristic features of persistent pyrexia, cardiac valvular disease, anæmia, optic neuritis, and enlarged spleen were seen clinically; while, after death, there was found to be an extensive lesion of the mitral valve, with rupture of the chordæ tendineæ, and abundant fungating granulations on the surface of the left auricle. Micro-organisms had been found in the vegetations by Dr. Pitt. With regard to the etiology of the disease, observations were more and more tending to confirm the views of those who believed that ulcerative or septic endocarditis was not due to one particular organism, but might result from the invasion of the organisms of different diseases. According to MM. Lion and Martineau, there had been found in cases of septic endocarditis the organisms of septicæmia and pyæmia, those of pneumonia, typhoid fever, and tuberculosis, as well as six others not found in other diseases. In different cases the valves might be differently affected according to the particular organisms concerned. Clinically, it became of the greatest interest to note the diseases with which any case of ulcerative endocarditis was associated as bearing upon its course and complications. Thus it had been noted by more than one observer that septic endocarditis following pneumonia attacked especially the aortic valves, and was sometimes accompanied by suppurative meningitis. Such a case had happened at Guy's Hospital comparatively recently. Dealing with the symptoms, Dr. Taylor called attention to the cardiac murmurs, the pyrexia, and the evidences of embolic processes, and discussed points connected with them. He pointed out the long duration of the pyrexia which was seen in some cases, extending, for instance, to six months in the case above quoted, during which the fever was almost absolutely regular, the temperature rising at night and falling in the morning. The evidences of obstruction he dealt with under six heads,—(*a*) absence of pulsation in accessible vessels; (*b*) loss of function of vessels not accessible,—for example, hemiplegia from blocking of a middle cerebral; (*c*) disturbed function, such as albuminuria; (*d*) obvious infarcts, as shown by the enlargement of the spleen in some cases; (*e*) hemorrhages,—of some of these he suggested that they might not be embolic, but rather stand to the bacterial virus of endocarditis in the same relation as the petechiæ of small-pox and typhus did to the virus of those diseases,—namely, they might be toxic in origin; (*f*) inflammatory lesions, such as optic neuritis and nephritis; their relation to embolic processes was uncertain. Among the various symptoms of this disease, special stress was laid upon anæmia and optic neuritis. Anæmia was very frequent, and had some diagnostic value. Optic neuritis occurred with greater frequency in this disease than in typhoid fever, with which it was apt to be confounded.

NEPHRITIS IN CONSUMPTION.

In the *Centralblatt für Allgemeine Pathologie*, No. 3, 1891, Dr. C. V. Kahlden, of Freiburg, describes certain changes which he has observed in the kidneys of phthisical patients, apart from those brought about by actual tuberculous disease or amyloid degeneration. The whole organ is either not all or only very slightly enlarged; the capsule is easily separated from the yellowish-white surface; the cortex is but little narrowed,

but invariably shows a slight yellowish discoloration; the medullary tissue is usually pale and anæmic. A case of chronic phthisis is related, and full details given of the microscopic appearances corresponding to the yellow changes in the cortex. The clinical evidence of these changes is very limited. Albuminuria may be altogether absent, or only present at irregular intervals in minute quantity. There is, as a rule, no hypertrophy of the heart and very little œdema of the extremities. The actual changes within the kidney consist for the most part of an irregular aggregation of small round cells within the capsule of the glomeruli, the cells themselves showing minute fatty changes. The endothelial cells lining the tubules show a certain amount of fatty change, and small granular cells are scattered in the intertubular tissue also; but the distinctive difference claimed for this form of degeneration over others that are recognized as occurring in chronic phthisis is the occasional limitation of the degenerative process to the endothelium of the tubules, the interstitial tissue being but little altered. The changes are looked upon as essentially degenerative in nature and as prone to affect the parenchyma of the organ in the first instance. The author discusses the arguments for and against this view at considerable length, and concludes that such parenchymatous changes in the kidney in cases of long-standing chronic phthisis are the rule rather than the exception.—*British Medical Journal*, March 7, 1891.

THE SYMPTOMS OF MYXŒDEMA AND EXOPHTHALMIC GOITRE.

At the meeting of the Edinburgh Medico-Chirurgical Society, held March 3, 1891, Dr. Bramwell read a paper, in which he contrasted the symptoms of myxœdema and exophthalmic goitre (*Medical Press and Circular*, March 11, 1891). In both of these affections the thyroid gland was affected. In the former it was atrophied and its functions diminished, while in the latter it became hypertrophied and its functions increased. In myxœdema the symptoms came on in a slow and insidious way, generally late in life, and usually in married women; in exophthalmos they often set in suddenly, as after a fright, earlier in life, and in unmarried, or, if married, sterile women. The temperature in myxœdema was subnormal, and patients felt cold, the skin was dry and harsh, and its electrical resistance increased; in exophthalmos the temperature was subject to elevations, the skin soft and moist, and its electrical resistance diminished. Constipation and amenorrhœa were usually present in the former affection, while in the latter diarrhœa and menorrhagia were frequently met with. Nervousness was not present in myxœdema, but was a constant symptom in exophthalmos. Myxœdema was said to be the result of degeneration of the thyroid gland, and might be secondary to some nerve lesion. In cases where the thyroid became atrophied or its functions diminished, or where it had been extirpated, these symptoms of myxœdema appeared. The symptoms of exophthalmos, on the other hand, were the result of excessive activity of the function of the thyroid, or might be due to perverted function of the gland. The pathology of exophthalmos was obscure, but the primary cause was apparently nervous, and due to some derangement of nerve-centres.

BACTERIA IN THE SALIVA IN CASES OF MEASLES.

Drs. H. Mery and P. Boulloche, as results of their bacteriological studies made with saliva of children suffering from measles, offer the following statements (*Revue Mensuelle des Maladies de l'Enfance*, April, 1891):

The pneumococcus and streptococcus are met with in the saliva of children suffering from measles with much greater frequency than is the case in health. Broncho-pulmonary complications in the course of measles only occur with but rare exceptions in children in whom the saliva contains the pneumococcus and streptococcus. At the autopsy in fatal cases it is possible to follow the pathogenic microbes recognized in the saliva throughout the upper air-passages down to the finer bronchi. The frequent presence of the pathogenic microbe in children suffering from measles serves to explain the great frequency of broncho-pulmonary inflammations in such cases. The practical deduction to be drawn from this conclusion is that during the progress of a case of measles the most rigorous attention should be paid to buccal antisepsis.

INTERLOBAR PLEURISY.

Professor Potain contributes a paper to *L'Union Médicale*, No. 27, 1891, dealing with the subject of interlobar pleuritic effusions. A typical case is recorded where pus is periodically evacuated through the bronchi,

and in which there are evident signs of fluid effusion in front of the upper lobe of the left lung, but not in the general pleural cavity, the fluid being probably localized by firm adhesions. The diagnosis of such cases is always difficult, and a localized collection of fluid may frequently be mistaken for a solid mass unless due precautions are taken. They commonly occur as interlobar effusions or as effusions between the lung and the diaphragm. In either case they are almost always purulent. The occurrence of frequent rigors and a dry cough, if not due to congestion or accompanied by signs of a general pleurisy, should always suggest the possibility of interlobar effusion. Physical signs may not at first be present, but show themselves as the fluid approaches the surface. It is usually evacuated through the bronchi, setting up a certain amount of irritative bronchitis in the process. The opening into the lung is usually small and irregular, and it is rare for air to escape from the lung into the abscess cavity. In cases where such escape does take place, it generally happens that putrefactive changes are set up in the fluid which remains behind, and this necessitates an operation to evacuate and disinfect the cavity. In cases such as the one related, where there is no evidence of change taking place in the pent-up fluid, no operative measures are proposed. Unlike a general empyema, the interlobar form shows a marked tendency to spontaneous cure.—*British Medical Journal*, April 4, 1891.

HYDROCHLORATE OF AMMONIUM BY INHALATION IN MEMBRANOUS CROUP.

In the *Medical Record* for April 11, 1891, Dr. Dwight L. Hubbard calls attention to the use of hydrochlorate of ammonium in laryngismus stridulus and laryngo-tracheal diphtheria.

Dr. Hubbard believes that this ammonium salt is of value, in the first place, as a heart stimulant, producing better oxidation of the blood, by bringing it in more frequent contact with the inspired air; second, in relieving the spasm and œdema of the glottis; and, third, in softening the false membrane. His method of employing this remedy is to place the patient in a small closed room, having a temperature of about 80° F., then generating sufficient heat to drive off copious fumes. This is continued for fifteen minutes, and repeated every hour; while after each application the room should be ventilated as much as possible without reducing its temperature. Dr. Hubbard writes that, after the use of this remedy so employed copious perspiration follows, the breathing becomes less stridulous, the mucus softer and more easily expectorated, and sleep generally is produced.

THE PHYSIOLOGICAL EFFECTS OF TRIMETHYLAMINE.

At the meeting of the Société de Biologie, held March 15, 1891, Drs. Combemale and Brunelle (*Le Progrès Médical*, March 21, 1891) reported that, whether given by the stomach, subcutaneously, or by inhalation, the immediate effect of the administration of trimethylamine is to excite excessive secretion of saliva and increase of its normal alkalinity. In addition to these constant symptoms there is frequently also an increased secretion of the nasal mucus and the lachrymal secretion, while small quantities of albumen can usually be detected in the urine for several days after the administration of trimethylamine. Injected under the skin in watery solution weaker than one-half of one per cent., it produces sloughs and ulcers which are extremely indolent in healing. In the strength of one-half of a grain for every two pounds of body-weight, there is always a reduction of temperature, while at the same time there is an increase in the rate of pulsation of the heart. The minimum fatal dose is about five grains for every two pounds of body-weight.

THE COLD-BATH TREATMENT IN TYPHOID FEVER.

But little has recently been heard as to the treatment of typhoid fever by cold bathing. The general opinion has, however, been frequently expressed that to settle the value of this method of treatment two carefully-recorded series of cases should be published, the one treated in the ordinary way, expectantly, and the other treated systematically, without selection, to cold bathing; each series to be consecutive and sufficiently long to eliminate chance mortalities, and the two to be strictly comparable in all respects save only the one item of treatment. These conditions are, we believe, fulfilled in a paper published in the *Practitioner* for March, 1891, by Dr. F. E. Hare, from the analysis of the cases occurring under his care in the last five years in the Brisbane Hospital, Queensland. It seems that Dr. Hare has had exceptional opportu-

nities for the study of this disease, as judged by the excessively large number of cases which have been admitted into the hospital. He writes that from August 1, 1885, to December 1, 1886, there were five hundred and eighty-six cases of typhoid fever admitted to the hospital. During most of the time the treatment was merely expectant, although at the latter part of this period—sixteen months—quinine was rather freely used in antipyretic doses. Not more than two or three cases were bathed, but cold sponging was frequently used, and the cold wet sheet not uncommonly, in cases of high temperature. Of these five hundred and eighty-six, eighty-five died, giving a percentage mortality of 14.5. Comparing these figures with the records of typhoid fever cases admitted to this hospital from May 15, 1882, up to December 31, 1886, eighteen hundred and twenty-eight cases have been treated in the hospital, of which two hundred and seventy-one had proved fatal, giving a mortality percentage, therefore, of 14.82. It therefore seems that the percentage of deaths occurring in this series of cases might be fairly taken as giving an average mortality from the ordinary hospital expectant method of treatment of typhoid fever, and Dr. Hare uses this as a control list to compare with the results of the cold-bath treatment. For the three years during which the cold-bath treatment was systematically employed eleven hundred and seventy-three cases were admitted. Of these, ninety-two died, thus making the percentage mortality 7.84. In other words, under the bath treatment there was an improvement in the hospital mortality almost amounting to fifty per cent. The treatment consisted in the strict application of Brand's rule, which is, briefly, a cold bath (68° F.) of about fifteen minutes' duration every three hours, day and night, should the rectal temperature reach 102.2° F. Of course, a considerable number of milder cases do not require this uniform bathing, from failure of the temperature to attain this height. In addition to the bathing, quinine was occasionally given in antipyretic doses of 3, 5, and 7 grains. Occasionally, also, it is stated that antifebrin was given in 5 grains, where the temperature was especially obstinate to the bath.

The diet consisted of milk and beef-tea; whiskey was given in severe cases, but after the value of quinine as a cardiac stimulant was recognized, rarely more than six ounces of whiskey were found necessary even in the severest cases. Diarrhœa, meteorism, and hemorrhage were treated by constant appliion of ice-bags to the abdomen. The mere statement of the reduction of mortality in these two series of cases cannot by itself claim the fullest confidence in the character of the results, for every such conclusion is open to the objection, in the first place, of an insufficient number of observations; 2, variations in the extension of the term typhoid; 3, variations in the severity of the disease in different countries, climates, and districts, and in different epidemics in the same place; also differences in the age and sex constitution of the series compared; and, finally, errors in diagnosis.

Dr. Hare has, however, considered all of these possible objections, and has, we think, successfully eliminated various fallacies which might occur in such an investigation. As regards the first of these,—as to the number of cases,—it is evident that, roughly speaking, the number required on which to base any reliable conclusions in any disease will vary inversely in the standard mortality of the disease in question. In acute traumatic tetanus, an almost invariably fatal affection, a very few successful cases would be enough; with a disease whose standard mortality was fifty per cent., the list would have to be considerably extended; while in the case of typhoid, in which the majority attacked recover under any treatment, or even in spite of treatment that is positively bad, a very large number of cases would be required. To show the value of his series of typhoid cases, Dr. Hare groups the eighteen hundred cases into four different series of various sizes, each being consecutive in the order of admission, whose average mortality was 14 9 per cent. He finds that, as might be expected, in the small groups, say of one hundred, there being great variation in the character of the affection, in eighteen of such groups the percentage mortality varied from eight to twenty-two per cent.; in other words, giving a variation of fourteen per cent.; while, when he grouped the cases into three series of six hundred each, there was only one per cent. of variation in mortality. Therefore, the first objection seems to be answered,—that is, in this series of cases the probable error in percentage mortality attributable to variations in the intensity of the disease is insignificant. As regards the second possible error in the extension of the term typhoid, the objection here is somewhat similar to that which occurs under the fourth head of errors in diagnosis. The inclusion in typhoid tables of the milder and indefinite varieties of fever, such as febric-

ula, simple continued fever, etc., is a recent and to some extent justifiable tendency, and yet for statistical purposes it is evident that some definite standard is required. Great difficulty was at first experienced in the classification, and in many instances fatal cases of unmistakable true typhoid fever were not infrequently noted where diarrhœa, meteorism, abdominal symptoms generally, and even the rash were absent.

Dr. Hare therefore determined in this classification to take the duration of the pyrexia as a basis, since in Brisbane typhus fever is unknown and malaria met with only in its intermittent form, typhoid is practically the only fever that exists. Accordingly, Dr. Hare states that all cases that convalesced the tenth day of the fever were excluded, even although undoubtedly many of these were of a typhoid nature. Dr. Hare then makes four divisions, —the first group including all cases usually termed typhoid, simple continued fever; the second excluding cases that convalesced before the tenth day; the third excluding cases that convalesced before the fifteenth day; the fourth excluding cases that convalesced before the twentieth day, and always including fatal cases. According to the expectant treatment, percentage mortality of his cases in the first group was 12.59; under the bath treatment, the same class, 6.69. In the second group, the percentage mortality under expectant treatment was 14.50; under the bath treatment, 7.84. In the third group, under expectant treatment, 16.50; under the bath treatment, 9.29. In the fourth group, percentage mortality under the expectant treatment was 20.09; under the bath treatment, 11.92. Thus it is seen that in all of these groups there is a percentage reduction in mortality in favor of the bath treatment of nearly fifty per cent. The possible variations in disease, owing to the severity of the climate and other local causes, have not in the present instance any importance, since all the cases in each series came from the same districts and were treated in the same wards.

Sex constitution varies but slightly from year to year, and in long series is practically identical. Of the eighteen hundred and twenty-eight cases expectantly treated, six hundred and sixty-eight, or 36.54 per cent., were females; of the eleven hundred and seventy three in the bath period, four hundred and thirty-four, or 36.99 per cent., were females. Sex constitution has, however, a powerful influence upon the success of the bath treatment, as will appear later.

Age constitution is of less importance in typhoid than many other diseases. Only at the two extremes of life is its influence at all considerable, the mortality being lowest under 10 and highest over 40. Of the five hundred and eighty-six cases in the expectant period, 1.08 per cent. were under 10, and 4.33 per cent. over 40. Of the eleven hundred and seventy-three in the bath period, .68 only were under 10, and 6.48 over 40. So far, therefore, age constitution would tell against the latter period, but practically its influence may be neglected.

With regard to variations in severity in different epidemics, seasons, etc., it has been urged that the reduced death-rate at the Brisbane Hospital during the three years' bath period is largely, if not wholly, due to the type of the disease having become milder. Were this true, similar variations should have been met with previously. But it has been shown that such variations only occurred in the smaller series, disappearing almost entirely in those containing six hundred and upward.

Similarly, it can be shown that whatever variations existed in the different *fever seasons*, before the introduction of the bath treatment, were but slight. In Queensland, the prevalence of typhoid follows almost exactly the same rule as in England, being at its minimum in the spring month of September, at its maximum in the autumn month of March. Consequently, if we take the year between September and September, we shall include the whole of a single fever season.

The annexed table shows the death-rates of the four complete fever seasons before the introduction of the bath treatment:

TABLE.

Season.	No. of cases.	Deaths.	Percentage mortality.
September, 1882, to September, 1883...	222	29	13.06
September, 1883, to September, 1884...	568	88	15.49
September, 1884, to September, 1885...	399	58	14.54
September, 1885, to September, 1886...	457	69	15.10

From this it appears that the natural seasonal variations were inconsiderable, and, if we except the first, containing but two hundred and twenty-two cases, did not amount to one per cent. The presumption, therefore, is, that during the succeeding three years the

type remained fairly constant, in the absence, of course, of any evidence to the contrary.

Now, to point to the lower fatality of the disease as a proof of its greater mildness is to ignore the question of treatment,—the point at issue. Such an argument, of course, is simply begging the question, and is logically absurd. But, apart from this, it is very difficult to adduce any facts in support of the theory of alteration in type.

On the other hand, there is a considerable amount of evidence pointing in the opposite direction. On comparing the two periods, it is found that, omitting relapses, the average duration of cases that recovered (where it was possible to fix the date of onset) was almost identical in each, being 23.8 days in the expectant and 24.3 days in the bath period. But by far the most conclusive argument in favor of the identity of type of the two series is found on analyzing the immediate causes of death. Here will be shown that certain complications and accidents, notably intestinal hemorrhage and perforation, which bath treatment could scarcely be expected *a priori* to prevent, have been almost equally frequent in either. To further support the contention, therefore, it would be necessary to assume that the change of type was of so selective a nature, that while it greatly reduced the general mortality of the disease, it left the dangers arising from the intestinal lesion practically unaffected.

Finally, as to the fourth possible fallacy in the value of such conclusions,—that is, as to the fact that the diagnosis is to be made so early that there is no certainty as to its correctness. This objection, however, scarcely applies to these series, for this diagnosis is here not made at the beginning but at the termination of the case; accordingly, the bath was used in all febrile cases which were sufficiently severe, while the diagnosis, and therefore the grouping of the cases in the series, was only regarded in successful cases after their discharge after a careful review of the history, chart, and clinical notes, and in fatal cases after the autopsy. Of course, then, it follows that, in a long series of cases, many other diseases than typhoid would be treated; although many of this disease have been benefited by the bath treatment, they are not included in Dr. Hare's tables. Again, in every such series of cases there must be a great number of cases which are doomed under any circumstances, and these must to a great extent obscure the effect of treatment.

Thus, of the ninety-two fatal cases that occurred during the bath period, eight took place in less than fifty hours from admission, and two more in less than seventy-two, while in seven others the treatment was deemed inapplicable for various reasons. These were, in four, extreme prostration either from pre-existing disease (fatty heart, old hip-disease, and senile decay) or complications present on admission (acute nephritis), in three the fact that the disease was not diagnosticated during life. Of these latter, one had numerous articular abscesses, with a history of acute rheumatism, one was thought to be acute phthisis, and the other was admitted with all the symptoms of dysentery. The last died from perforation of the rectum, and the autopsy showed that the dysentery had been secondary to a recent attack of typhoid.

In yet two other cases death was but very indirectly due to the fever. In one acute cystitis developed, being probably due to a dirty catheter; in the other, an ineffectual attempt to pass an instrument through a tight urethral stricture caused rigors, hyperpyrexia, and death. In this case the bladder was found post mortem to have a capacity of only five ounces, and the walls to be enormously thickened, while in both the intestinal ulceration was practically healed.

Excluding, therefore, these nineteen cases, as not bearing upon the question of treatment, the hospital mortality for the three years, extending over a series of eleven hundred and fifty-four cases, falls to 6.33 per cent.

Hitherto the influence on the general mortality only has been considered, but this is obviously inadequate in dealing with a disease where death threatens from so many directions. The two ever-present dangers are (1) the pyrexia, common to all continued fevers, and (2) the intestinal lesion, peculiar to enteric; and to either, or both of these, most of the deaths might be referred. *A priori* it could hardly be expected that the treatment would influence the latter, at any rate favorably, and therefore it is in the highest degree desirable to settle the point by statistics.

Unfortunately, a difficulty here arises,—death is so frequently due to a co-operation of the pyrexia and the intestinal lesion, that it is manifestly incorrect in many cases to attribute it solely to either. Especially is this so where diarrhœa, meteorism, and other abdominal symptoms have coexisted with prolonged high temperature.

There are, however, two modes of death,—viz., perforation and hemorrhage,—which should properly be regarded as incidents,

inasmuch as they are the result of the depth of the ulcer, and not of anything in its specific nature. They are, at any rate, undoubtedly due to the intestinal lesion and to it alone. Consequently, no question of classification need arise to prevent their relative frequency in the two series from being determined statistically.

Of the five hundred and eighty-six cases treated expectantly, seventeen died from perforation and eleven from hemorrhage. The percentage mortality (to total cases), therefore, of each accident was 2.90 and 1.88, respectively, or together, 4.78.

Of the eleven hundred and seventy-three cases during the bath period, thirty-four died from perforation and sixteen from hemorrhage. The percentage mortality of each, therefore, was 2.90 and 1.36, respectively, or together, 4.26.

Hence it is plain (1) that, instead of being more common under the bath treatment, as many have feared, death from these two complications has been actually, though slightly, less frequent; and (2) that the decrease, such as it is, is altogether due to the diminished frequency of fatal hemorrhage.

It is to be observed that the figures quoted relate to the mortality caused by these accidents and not to the frequency of their occurrence. In the case of perforation, which is almost of necessity fatal, the distinction is without importance, but it is otherwise with hemorrhage, which, as a matter of fact, has occurred as frequently (though not more so) under the bath treatment as before. Its diminished mortality is, no doubt, to be explained by the fact that the patients have been in better condition at its onset, and therefore the better able to recover from the loss of blood.

The conclusion, therefore, is that the treatment has no effect upon the occurrence of perforation or hemorrhage, one way or the other, but that it renders the latter slightly less dangerous.

Modes of Death other than the above.—Obviously it is among these that the main source of the reduced general mortality must be sought.

During the expectant period the deaths under this head were fifty-seven; their mortality to total cases, 9.73 per cent.

During the bath period they numbered forty-two, their mortality being, therefore, 3.58 per cent. Here, then, is a reduction amounting to over sixty-three per cent.

Now, some of the causes of death in this list are well defined and undoubtedly "pyrexial" in origin, inasmuch as they are liable to arise in any severe continued fever. They are:

a. Chest affections,—*e.g.*, pneumonia, empyema, etc. Simple hypostatic congestion of the lungs is not here included.

b. Cerebral affections,—*e.g.*, acute mania, general convulsions, apoplexy, etc.

a. Fatal chest affections have thus been less than one-fourth as frequent. Of the six in the bath period, one was from empyema, which had become chronic, and proved fatal six months after the subsidence of the fever; three from acute lobar pneumonia, in all of which the complication developed suddenly and rapidly, and carried off the patient; and two only were from broncho-pneumonia, in one of which it was present on admission, and led to a wrong diagnosis.

In only one instance, therefore, during the bath period, did fatal broncho-pneumonia develop subsequently to admission.

The greater success attained in averting broncho-pneumonia, by means of the bath treatment, is quite in accord with what is known of the pathology of the disease. Its immediate antecedents are plugging of the terminal bronchioles and collapse of the lung-sacs, preceded in most instances by bronchial catarrh. Its development is favored by feebleness of the circulation, muscular prostration, and a state of mental torpor, during which the patient fails to appreciate the necessity of coughing. Consequently, it always occurs late in the disease.

The causation of the lobar variety seems more obscure. It is not usually preceded by bronchial catarrh, and it is liable to arise at any period in the disease, as often as not before there are any signs of cardiac failure, of which, indeed, it may be the immediate cause.

No surprise, then, need be felt that the bath treatment should be more effectual against the bronchial form, each immersion causing, as it does, increased intellectual clearness, deep inspirations, and powerful coughing efforts, followed by expectoration of any mucous plugs that may be blocking the tubes, besides acting undoubtedly as a powerful prophylactic against circulatory failure.

b. The deaths in this class are only those in which some well-marked cerebral complication developed at a time when as yet no other threatening symptoms had appeared; in which death rapidly followed, and in which, therefore, it is fair to assume that it

proceeded chiefly, if not solely, from the brain. These cases were acute mania, general convulsions, apoplexy from subarachnoid hemorrhage, and one unusual case of coma.

Although the mortality in this class is seen to have fallen to exactly one-quarter, yet the cases are too few to be in themselves conclusive. For this reason Dr. Hare has added an analysis of the cerebral *symptoms*. These, by which are meant the ordinary forms of delirium, stupor, etc., but rarely prove fatal directly, yet without doubt they are important contributory causes of death.

Of the nine hundred and thirty-four cases admitted during the years 1888 and 1889, delirium or stupor occurred in seventy-one, or in 7.60 per cent. only. Murchison found these symptoms present in sixty-seven per cent.

Even more convincing, however, is a consideration of the circumstances under which the symptoms arose in these seventy-one cases. All the cases of stupor (nine), and twenty-five of those delirious, were so on admission. Of the remainder, twenty-four became delirious for the first time, only after the bathing was stopped for various reasons. Such reasons were, in some instances, the onset of a contraindicating complication (hemorrhage, perforation); in others, simply a falling temperature, which rendered the continuation of the treatment unnecessary, and which, in fact, indicated the approach of convalescence. Two more cases were not bathed at all. There remain only eleven, therefore, out of the nine hundred and thirty-four cases in which any kind of mental disturbance arose during the continuance of the bathing, and where, consequently, it may be said to have occurred in spite of it.

c. The mortality of this class is seen to have been reduced from 6.82 per cent. to 2.89, or nearly fifty-eight per cent. It constitutes, as already said, a residuum. In it are included most of the causes of death termed pyrexial, together with others due to the intestinal lesion. No accurate comparison can, however, be made between the two periods, for two reasons,—1, because the distinctions between the influence of the lesion and of the pyrexia are not always sharply defined; and, 2, because during the expectant period, the record was not sufficiently minute.

Analyzing the thirty-four cases in the bath period, it seems that some cases hardly bear upon the treatment at all. Thus three died from abortion, while in five death was due to altogether exceptional causes or clearly dependent upon pre-existing disease. In twelve cases the intestinal lesion seemed the most important factor; in three of six, exhaustion seemed to be the immediate cause of profuse diarrhœa, showing a more favorable percentage than was met with in the series of cases treated by the expectant method, while in the remaining nine cases death undoubtedly resulted from dysentery. There yet remains fourteen cases in which there was no special discoverable cause for death, and in which the fatal event, therefore, must be attributed simply to pyrexial cardiac failure. This also was a much more prominent cause of death during the series treated by the expectant plan; and, in fact, it seems in rendering this source of death infrequent that the bath treatment is so eminently efficacious. In support of this, it will be found on examination that most of the fourteen cases in this group were admitted under circumstances that were highly unfavorable.

Thus no less than four were practically moribund on admission and died within seventy-two hours; four were admitted during the fourth week of the fever or later, two during the third, two during the second, and two only before the end of the first. The significance of this can be appreciated when it is known that more than fifty-three per cent. of the total cases were admitted during the first week of the disease. Dr. Hare believes that his records warrant the statement that this mode of death was five times more prevalent in the series of cases treated under the expectant plan than in those in which the bath treatment was rigorously followed.

Again, Dr. Hare lays the greatest stress upon an absolutely strict adherence to Brand's rule, already referred to.

Finally, after discussing the influence of delayed admission upon the hospital death-rate of typhoid, and on the variation in mortality in the two series, the author summarizes his conclusions as follows:

1. That by means of the bath treatment, systematically employed, the hospital death-rate of typhoid may be greatly reduced.

2. That the reduction should amount to fifty per cent. on the previous death-rate; and that the percentage mortality to admissions should not be over eight per cent. (always supposing the term *typhoid* to be used in its second degree of extension).

3. That this result may be obtained in spite of the fact that many of the cases are unsuited to the treatment, and that much more might be expected in appropriate cases only.

4. That the success is in proportion as the treatment is begun early in the disease.

5. That, as evidenced by the undiminished occurrence of perforation and hemorrhage, and by the fact that early admission has failed to render them less frequent, the treatment has no influence on the depth of the ulceration.

6. That, since a constant percentage (about four and a quarter) of the cases admitted die from these accidents, no reduction in the general mortality much below five per cent. can be expected from the treatment, even were it possible to insure every case being admitted under the most favorable circumstances.

7. That, as the result of the different liability of the sexes to these accidents, the prognosis under the bath treatment is vastly more favorable in females than in males. For instance, in any two given cases, *cæteris paribus* and without reference to the date of fever on admission, the danger to life is but little more than half in the case of the former; while if both are admitted during the first week of the fever, this is reduced to one-quarter.

8. That, on the whole, the lethal influence of the intestinal lesion is diminished; that the treatment affects this (*a*) directly, by moderating diarrhœa, and (*b*) indirectly, by sustaining the powers of the patient, and thereby enabling him to recover from the effects of the hemorrhage and other not necessarily fatal intestinal conditions.

9. That the vast bulk of the reduction in mortality is due to the prevention of those complications and modes of death which, being more or less common to the febrile state, however induced, have been termed pyrexial. Thus (*a*) fatal pneumonia has been less than one-fourth as frequent, this being chiefly due to the rarity of the bronchial form; (*b*) brain complications have been less fatal, and brain symptoms (delirium, stupor, etc.), enormously reduced in frequency; while (*c*) it is no exaggeration to say that simple cardiac failure would have been practically expunged from the list had all the cases admitted come under treatment during the first week of the disease.

This last conclusion (9) embodies the central truth brought out by the inquiry. For those who are inclined to withhold their assent from it, only one loop-hole remains open, and that is a doubt as to the good faith of the statistician. To meet this to some extent, the original documents which constitute the data of the inquiry have been preserved and filed at the Brisbane Hospital, where they may be examined by any member of the profession who is sufficiently interested in the subject. They include,—1. Most of the charts of the cases in the expectant period. 2. All the charts (with three or four exceptions) in the bath period, with a brief account of the main features in each case, the number and duration of the baths, and their effect on temperature and pulse, and other special therapeutic measures. 3. Post-mortem record, consisting of notes made at the autopsy on one hundred and seventeen of the fatal cases; eighty-seven are from the bath period, no examination being made in the other five. Thirty are from the expectant period. Although post-mortem examinations were only omitted in about seven of the eighty-five fatal cases that occurred in this period, unfortunately the record of the earlier ones was not preserved.

HYPODERMIC INJECTIONS OF GUAIACOL IN PHTHISIS.

Professor Picot, of Bordeaux (*Semaine Médicale*, March 4, 1891), reports the results of therapeutic experiments made during a period of two months in the Hôpital S. André in the treatment of pulmonary tuberculosis and pleurisy of tuberculous origin. He prefaces his report with a declaration that he does not pretend to cure tuberculosis, but only records certain results which he has in certain cases seen follow the use of a solution of guaiacol and iodoform in perfectly sterilized olive oil and vaseline. Each cubic centimetre of the fluid, which is perfectly pure and transparent, contains one centigramme of iodoform and five centigrammes of guaiacol. The supraspinous fossæ were chosen as the seat of injection, as there is not much movement in that region, and it does not bear the weight of the body when the patient lies on his back. The initial dose was 1 cubic centimetre, which was gradually increased to 3; no swelling or other local reaction was ever observed at the site of puncture. In about one case in twenty a certain amount of numbness was felt in the shoulder of the same side after an infection, but this always disappeared in from five to six hours. That the substance injected is absorbed was proved by the fact that iodide of potassium was eliminated in the urine. A small quantity of iodide of potassium was also found in the lungs of a patient who died during treatment. The only sign of general reaction is profuse perspiration, especially of the face and chest, which comes on, as a rule, from twenty to thirty

minutes after the injection. The cessation of the sweating is followed, as a rule, by a fall of temperature from .5° to 1° C. The injections did not affect the digestion, but in some cases, when the treatment had been carried out for a week or ten days, slight colic and diarrhœa were complained of; these symptoms ceased on discontinuing the injections. No effect on the urine was observed. With the view of determining whether the remedy could give rise to fresh crops of tubercles, Dr. Picot used the injections "in three phthisical subjects in whom the considerable lesions could not be checked in their progress, and who were likely at an early date to allow of the wished-for anatomo-pathological examination." One of these, a man, aged 55, with cavities at both apices, received thirteen injections between January 28 and February 10. He died on February 11, and at the necropsy "it was easy to see that neither in the lung nor in the intestine were there recent crops of tubercles nor any submiliary granulation." Another patient, aged 19, both of whose lungs were riddled with cavities, underwent a series of injections from January 16 to 31. He died on February 21, and no recent granulations or submiliary tubercles were found. The third case gave similar results. These post-mortem examinations proved that the injections do not set up congestion around old tuberculous foci nor in the interior of cavities, and hence that there is no danger of their causing inflammation of the pulmonary tissue or hæmoptysis. The total number of patients treated has been twenty-five (fifteen men and ten women). Of these, as already said, three died "from the natural consequences of pulmonary phthisis which had reached the last stage." Even in these, however, some little objective improvement was noted, especially in the quantity of expectoration. It was remarked at the post-mortem on these cases that the cavities contained neither caseous material nor pus. In one of the cases in which there were tuberculous ulcers in the intestine, these showed signs of commencing cicatrization. In the remaining twenty-two cases the existence of phthisis was absolutely proved, both by the physical signs and by the presence of bacilli in the sputum. In two cases "with manifest cavities" and other signs of advanced phthisis, the treatment was followed by almost immediate improvement; expectoration and cough ceased, the temperature became normal, night-sweats disappeared, appetite returned, and weight was gained. In one of these cases the physical signs were so modified as to indicate that the excavations were much diminished in size. The bacilli were much fewer in one case; in the other, as there was no expectoration, nothing could be said as to this point. In six other cases of phthisis in the second stage, the results were still more remarkable. These and the other cases treated will be published by Professor Picot in full detail. During the thirteen years he has been teaching at Bordeaux he has never before obtained such results from any kind of treatment. The cases of pleurisy treated in the same way were eight in number; five of these are still under treatment, and show marked improvement; three have been discharged "cured." Professor Picot sums up the effect of his remedy as follows: The injections improve the general condition, and lessen cough and expectoration. In certain cases they dry up cavities and favor their cicatrization. In the second stage of phthisis they make cough and expectoration disappear, while causing the cessation of fever and night-sweats. They also diminish the number of bacilli in the sputum. Whether this is "cure" or not, time and clinical experience alone can show. Dr. Picot thinks a tuberculous patient should be watched for five or six—perhaps even ten—years before he is pronounced to be cured.—*British Medical Journal*, March 14, 1891.

A NEW OPERATION FOR THE RADICAL CURE OF VARICOCELE.

In the *Lancet* for March 7, 1891, Mr. William H. Bennett describes an operation for the radical cure of varicocele. An essential detail in the operation, after the vas deferens has been isolated in the customary way, is an application through an incision in the scrotal tissues of two ligatures placed at a distance from each other round the sheath. The only available sources of this additional blood-supply are (1) some outlying branches of the spermatic artery, one of which sometimes comes off high up, and so may easily escape division; (2) the artery of the vas deferens, which may not be injured, even though the duct itself be divided: and (3) some small but important anastomotic vessels passing from the subvaginal tissue, which, in cases of congenital hernia, are more than usually large and numerous, in consequence of the modified relation of the tunica vaginalis and the hernial sac. This additional supply, although sufficient under favorable circum-

stances to maintain adequate nutrition of the testicle, is, however, derived from vessels which are, as a rule, small and delicate; any inflammation, therefore, about the part would be sufficient to choke them, sloughing of the organ following as a necessary result. If, however, no inflammation occurs,—*i.e.*, if the wound remains aseptic,—the supply of blood is enough to prevent sloughing and subsequent atrophy. The immediate cause, then, of the death of the testicle, which happened in these cases in the days prior to the practice of surgical cleanliness, as the term is now interpreted, appears to have been not the mere division of the cord, but rather the inflammation and suppuration, one or both of which almost constantly followed upon it.

It is almost impossible to include the whole of the latter vessels in a ligature in a case of varicocele without also including the artery, unless an elaborate and tedious dissection be undertaken for the purpose. It therefore would seem probable that in the vast majority of operations for varicocele, in which the spermatic plexus of veins is divided, that the main trunk of the artery is also involved in the section. It is probable, however, that the belief commonly held, that the nutrition of the testicle is dependent almost entirely upon the integrity of the spermatic artery, led to the conclusion that in operations in which the spermatic veins were freely divided, the artery had escaped injury because no ill effect was necessarily produced upon the testicle. It was then easy to assume that the apparent safety of the vessel was due to its having been pushed aside with the vas deferens. The second point of interest is the effect of this division of the spermatic artery, together with the veins, upon the nutrition of the testicle. The isolated position of this organ, coupled with the accepted view just referred to, that its blood-supply depends almost entirely upon the long and slender spermatic artery, has given rise to the impression that its vitality is endangered by the division of this vessel, together with the spermatic plexus of veins, and that section of the spermatic artery, veins, and vas deferens—virtually the entire cord—is also followed by sloughing of the testis. So strongly is this view held by some practitioners that it is not uncommonly taught, in the event of the cord, including the vas deferens, being divided during an operation, that it is proper to remove the testis at once, not only on account of its having been rendered functionally useless, but especially because if it is left sloughing will surely follow. Mr. Bennett, however, maintains that, in regard to division of the spermatic artery with the veins no harm whatever need result, for the artery of the vas deferens, which is certain to have escaped injury, is by no means always an insignificant vessel, and generally sufficient, by its anastomoses with the spermatic, to prevent not only immediate necrosis of the testicle, but also immediate wasting, as it often receives assistance from other vessels. In support of this statement, Mr. Bennett claims that in numerous cases in which he has operated a portion of the spermatic artery could be demonstrated in the excised part of the cord, and that in none of these instances has there been the least suspicion of wasting. On the contrary, the testicle, when soft or small, has invariably become more natural in size and consistence, and certainly, in one instance, more perfect in a physiological sense. The immediate result of division of the vas deferens with the spermatic veins and artery, whether by accident or of necessity, is naturally to render the testicle functionally useless, as its duct has been severed; but the idea that sloughing of the organ necessarily ensues is certainly not correct. In support of this latter statement, Mr. Bennett publishes notes of three cases, which seem to prove the truth of this latter statement. The fact that the organ survives after such a serious interference with its fluid supply must lie in the fact that there exists a considerable arterial supply over and above that which need be involved in a section of the cord itself. The portion of the cord lying between these ligatures is then excised. The whole of the spermatic plexus of veins, with the exception occasionally of a small vessel lying remotely at the back, are contained within the sheath formed by this fascia, and one object of including it in the ligature is to insure the obliteration of the whole of the veins; for it is clear that if the ligatures are passed round the connective tissue sheath before the vessels are exposed, none of these can escape. Further, if the ligatures are passed in the manner described, not only are the veins with certainty included, but also the main trunk of the spermatic artery, in evidence of which it is the custom, when operating in hospital practice, to demonstrate the existence of a section of this artery in the excised portion of the cord. Two points of interest here arise: First, it is obvious that if the spermatic artery is included in the ligature, as it certainly is under these circumstances, the traditional teaching of the schools,

that the vas deferens when pushed aside carries the spermatic artery with it, is wrong. Practically this is so, for the artery does not go with the vas deferens when it is displaced, but remains either quite close to the spermatic veins, or, as commonly happens in varicocele, is actually surrounded by them.

Finally, the points to which Mr. Bennett especially calls attention may be summed up in the following sentences:

1. That the vas deferens having been displaced in the manner usually adopted in operations for varicocele, the spermatic artery does not accompany it, but remains with the spermatic veins. 2. That in cases of varicocele the division of the main trunk of the spermatic artery, together with the veins, if the ordinary principles of surgical cleanliness be observed, is not only harmless to the testicle, but probably aids in the ultimate relief of the affection by diminishing the pressure of blood going to the testis at the time when almost all the returning veins are suddenly obliterated. 3. That the division of the vas deferens, spermatic artery, and spermatic veins, which entails a section of apparently the whole cord, is not necessarily followed by sloughing, or even subsequent wasting of the testicle, provided that a perfectly aseptic condition of the wound is maintained.

THE NUTRITIVE VALUE OF RECTAL INJECTIONS OF EGG ALBUMEN.

The assertions of Voit and Bauer and Eichhorst to the effect that egg albumen is absorbed by the rectum only in the presence of a certain proportion of chloride of sodium, but is returned unaltered with the fæces if this reagent be absent, has led the author to investigate this point anew, and to make his observations on man, and not on dogs, as his predecessors had done. The experiments were planned with great care, and the quantity of albumen removed from the body, both by the urine and the fæces, was estimated. As the outcome of several series of experiments, the results of which show a great agreement, HUBER gives as his conclusion that egg albumen simply beaten up is absorbed by the rectum, but only in very small quantities, and consequently a nutrient enema of this kind possesses hardly any value. When, however, a certain amount of common salt is added (one gramme (15 grains) to each egg in the present series of experiments), the quantity of albumen absorbed is doubled. Peptonized egg albumen was absorbed in very slightly greater proportion than that treated with common salt. Of the albumen thus treated with salt, between sixty and seventy per cent. was absorbed, and we, therefore, have in this mixture an extremely valuable material for nutrient enemata.

In no case of Huber's were the enemata expelled; nor was albuminuria ever found to occur after their use.—*Medical Chronicle*, April, 1891.

THE TOXIC ACTION OF NICKEL-CARBONYL.

Nickel-carbonyl is a new substance obtained by DRS. MOND, LANG, and QUINCKE by passing a stream of carbonic oxide over finely-divided nickel, resulting from the reduction of the oxide of nickel by hydrogen. Its formula is $Ni(CO)_4$. This liquid is volatile at about 40° C., while its vapor detonates and undergoes spontaneous combustion. These authors reported at the meeting of the Société de Biologie, held March 21, 1890 (*Répertoire de Pharmacie*, April 10, 1891), that they had injected 5 minims of nickel-carbonyl into the veins of a dog with the production of death one hour later. In larger doses it produces instantaneous death. Instilled into the eye it acted as a caustic, but without producing immediate death, as it seemed to be only with difficulty absorbed. Nickel-carbonyl is difficult to handle, not on account of possible explosions, which are without practical danger, and are by no means violent, but because its vapors produce the most excruciating headache. It acts by displaying oxygen from hæmoglobin. It remains, however, to be determined whether the combination which it forms with hæmoglobin is a combination in which the oxide of carbonyl is alone interested, or as to whether one is formed in which the molecular group of nickel-carbonyl enters in its entirety.

THE CAUSE OF INFLUENZA.

The annual meeting of the Michigan State Board of Health was held at the Capitol, April 14, 1891. Professor Fall, Drs. Avery, Hazlewood, Vaughan, and Baker were present. Dr. Avery was re-elected President.

Dr. Baker reported that he had worked out the cause of influenza. He said its greatly-increased prevalence during the last three months is alarming, because so many other diseases follow that disease, and increase after it increases, the diseases which so increase being consumption, pneumonia,

cerebro-spinal meningitis, rheumatism, osteomyelitis, etc., influenza seeming to bring in its train all of these most important diseases. Dr. Baker explained the causation of influenza. He stated that the germs of influenza are generally at all times present, and the germs of pneumonia, tuberculosis, and of the other specific diseases are somewhat widely disseminated; but that there must be certain coincident meteorological conditions to irritate the throat and air-passages sufficiently to let the germs gain an entrance to the body. These meteorological conditions in this instance were the excessive prevalence of north and northeast winds, and the excessive amount of ozone during the past three months.

The prevention of influenza, and of the coincident rise in the other more dangerous diseases, has not been possible, because of ignorance of the causes. Now the causes are known, and the study of the measures for the prevention can begin.

Reviews.

A Compend of Human Anatomy. By Samuel O. L. Potter, A.M., M.D. Fifth edition, revised and enlarged.
Philadelphia: P. Blakiston, Son & Co., 1890.

While this edition has been greatly improved by the addition of numerous cuts, tables, and plates, particularly of the arterial and nervous systems, it can be no longer said, as of former editions, that it "closely follows Gray," as the last edition of that book has apparently not been consulted in the work before us. Various typographical errors which appeared in former editions have been corrected and the book enlarged, until it now numbers three hundred and fifteen pages.

It is unfortunate that a larger type and heavier paper have not been used, which, while they might have added to the bulk of the book, would have unquestionably also enhanced its value.

Transactions of the Texas State Medical Association, Twenty-second Annual Session, April, 1890.
Austin, Tex.: Eugene Van Boeckmann.

As usual, the "Transactions of the Texas Medical Association" contain many very valuable papers, among which may be mentioned a "Report of Five Cases of Intracranial Surgery," by Dr. H. L. Fountain; "Comminuted Fracture," by Dr. F. W. Powell; "Cancerous Breast Removed," by B. F. Brittain; "Cerebro-Spinal Meningitis," by J. D. Burch; and the "Treatment of Chronic Tubercular Consumption," by J. C. Smith.

Essentials of Anatomy. By Charles B. Nancrede, M.D. Third edition, revised and enlarged. Based upon the last edition of "Gray's Anatomy."
Philadelphia: W. B. Saunders, 1890.

The reputation of Dr. Charles B. Nancrede as a surgeon and anatomist renders any comment on his writings upon these subjects useless. The colored plates which have been introduced into this last edition, the editing of which was supervised by Dr. Edward Martin, have added materially to the value of the work. They are clear and well colored, and are anatomically correct, which, unfortunately, is not always the case with anatomical plates. As this book is one of "Saunders's Question Compends," it was, unfortunately, necessary to write it in the form of questions and answers. Dr. Nancrede has, however, inserted as few questions as was compatible with the nature of the work.

It is to be observed that many of the questions are not followed by a note of interrogation. The plates on "Osteology," with which the work ends, are taken from "Gray," and should prove a help to the student.

A Latin Grammar of Pharmacy and Medicine. By D. H. Robinson, Ph.G. With an Introduction by L. E. Sayre, Ph.G.
Philadelphia: P. Blakiston, Son & Co., 1890.

In this excellent little book the authors have endeavored successfully to present a great deal of knowledge in the smallest possible space. It is unfortunate that the students of pharmacy and of medicine should not have a sufficient acquaintance with the Latin language before commencing their studies to render such a book useless; but, as this is not the case, and as a knowledge of the rudiments of the Latin are of great service to professional men, we feel that we cannot do better than thoroughly recommend the work before us, fearing, at the same time, that few students possess the leisure or the inclination to study it as they should. H. M.

The Therapeutic Handy Reference-Book for Physicians. Third edition.
Philadelphia: William R. Warner & Co., 1890.

This little manual, now in its third edition, contains in convenient form much that is of value to the practitioner of medicine. The rules for prescription-writing are followed by

tables showing the equivalences of apothecary's weight and the metric system, from grains and drops to ounces and gallons. The chapter upon poisons and their antidotes has been carefully revised and brought down to date. The tables of doses are very complete. The work concludes with a valuable formulary, where each prescription is placed under the disease for which it is useful. Many of these formulæ are the standard prescriptions used by well-known authorities in medicine from all parts of the world.

TEXT-BOOK OF MEDICAL JURISPRUDENCE AND TOXICOLOGY. By Jno. J. Reese, M.D., etc. Third edition, revised, and enlarged.
Philadelphia: P. Blakiston, Son & Co., 1891.

The third edition of Dr. Reese's work indicates that it possesses a hold upon the profession from its own intrinsic value, a view which is confirmed by a study of the book. Simplicity of style, conciseness, and directness of purpose have rendered it one of the best guides extant to the study of medical jurisprudence. The author has revised and somewhat enlarged it in the present edition, but it is still a compact, handy work, answering all the requirements of the student, except where recourse is necessary to the vastly larger works on the subject, which the newest medical library affords. E. W. W.

ANNUAL REPORT OF THE SUPERVISING SURGEON-GENERAL OF THE MARINE HOSPITAL SERVICE OF THE UNITED STATES FOR THE FISCAL YEAR 1890.
Washington: Government Printing-Office, 1890.

This report contains several papers of interest in the shape of reports. The opening pages contain a review of the progress of the "grippe epidemic," from which we learn that the earliest cases to be ascertained were observed in October, 1889, in Vjatka, Russia. To this there may be some objection, since it is well ascertained that the epidemic influenza existed in a distant but populous portion of the globe as far back as 1884–85. The report states that one fact is supported by general observation,—viz., its genesis in the north, and its dissemination by means of east winds. Ninety million persons are estimated to have been attacked in Europe in 1889–90, or about twenty-five per cent.; while in large cities one-half to two-thirds of the population suffered. The estimated mortality is enormous. Calling it one per cent., nearly a million deaths are laid to its charge; or at one-half per cent. even, and the figures are astounding, and the permanent sequelæ left will eventually largely increase the mortality. This estimate, it should be remembered, deals only with its first outbreak. The present recurrence is probably far more deadly. The report of the work done in the Hygienic Laboratory, United States Marine Hospital, New York, will be interesting to many. The "plasmodium malariæ" has been studied still further, and the results are confirmatory of the statement already made, "that malarial disease is contracted through the medium of food and drinking-water, the parasite gaining access to the system through the alimentary tract." This position established, calls for a considerable modification of our previous views, and also a change in our hygiene, which all should remember. The volume contains what seems to us only a medical curiosity, in the matter of the claim of Mr. F. A. Perroux, of Calcutta, as to the cure of cholera by inoculating with cobra venom. This claim is based upon the difference of action of cobra venom as compared with the venom of other serpents, and the fact that while lethal to cholera germs, its action does not in human beings coagulate the blood. A number of experiments on animals have been made, but the value of the venom as a cure for cholera fails to be established.

The book contains pictures and plans of many noted hospitals in Europe, and many reported cases of various forms of disease as noted in the hospitals of the service.

E. W. W.

SEXUAL NEURASTHENIA (NERVOUS EXHAUSTION): ITS HYGIENE, CAUSES, SYMPTOMS, AND TREATMENT, WITH A CHAPTER ON DIET FOR THE NERVOUS. By Geo. M. Beard, A.M., M.D., etc. Posthumous manuscript. Edited by A. D. Rockwell, A.M., M.D., etc. Third edition, with formulas.
New York: E. B. Treat, 1891.

The issue of a third edition of this book will again call attention to its value. Perhaps the author was a little too positive. He certainly was a little too advanced for his turn, but the book contains ideas of great value. His key-note is the discovery, which he seems to claim for himself, that sexual affections of the male organs are as much the cause of aberrations from health in the male as similar female sexual diseases are in her the causes and origin of a vast number of symptoms and conditions. At the present time medical fashion is drifting in two directions. It is abandoning the much-vexed uterus, and forbidding the endless detail of "treatment," so long in vogue. Yet it is still asserting its belief in deranged sexuality as a cause of dis-

ease by its growing ovariotomies and extirpations of organs. In short, it believes more than ever that the organs are offenders. It believes less and less in anything short of radical measures,—viz., their removal. So that while at first sight one might think that Dr. Beard's reasoning from analogy was less forcible than in the old days of the "irritable uterus," a closer view shows us that we still believe in the principle, and act upon it, only more vigorously.

Dr. Beard would explain by sexual derangement and functional diseases of these organs that vast mass of cases, growing daily more vast, where some hitherto unknown cause has deranged the functional perfection of the system. The break-downs, the nervous exhaustion, the special deviations from health in function, as well as the general collapse. Yet he gives a place for all the other acknowledged causes; in fact, sums them all up in the one word "civilization." These cause sexual neurasthenia. Yet it is by their action in deranging the sexual organs that he thinks he sees a hope of cure in his theory. "Civilization" is a great word and a greater fact, but one cannot attack it or cure it. The prostate gland is a much smaller fact, but amenable to treatment. Civilization, with its excesses, spirits, tobacco, wear and tear, deranges the prostate, the prostate deranges the man. Here is something definite to attack and something which we may hope to cure. Possibly the hope, as in the case of the gynæcologist, may prove illusive, and the androcologist of the future may be driven, like his brother of to-day, to extirpation. This specialty, by the irony of fate, will probably fall into the hands of the female practitioner, from whom radical measures may be expected.

The dryness of the American climate is by the author considered as the reason why neurasthenic diseases are more frequent among us. The extremes of heat and cold are also causes. These we acknowledge, but it is a question whether our climate be really dry. There is enough, however, to account, without this factor, for the abnormal strain under which we labor. Very probably transplantation of any race from its normal habitat leads to abnormal development. Possibly, by the fusion of races going on, as a vast experiment in our land, we are breeding a stock deficient in nervous stability. At all events, writers, both here and elsewhere, seem to acknowledge the fact, and agree with our author.

For the relief of what the author considers are the causes of neurasthenia, we must refer the reader to his own chapters. Electricity is his main reliance. Diet and regimen, with advice based upon the dictates of reason and common sense, supply the rest. One would err who classed this book with the great array of works on spermatorrhœa and impotence, which, after all, tell us so little. Dr. Beard had much to tell, as the reader will discover if he peruse this book with care.

E. W. W.

THE DAUGHTER: HER HEALTH, EDUCATION, AND WEDLOCK. HOMELY SUGGESTIONS FOR MOTHERS AND DAUGHTERS. By Wm. M. Capp, M.D. Philadelphia and London: F. A. Davis, 1891.

This is one of a large class of books concerning which little and much may be said. Little, for there is nothing absolutely new in it; much, for its old saws are well said, well selected, and can hardly be too often repeated. The book is full of good, common-sense advice. You can get it from other books, perhaps, but you certainly can from this. There are so many things about which the public never get accurate knowledge, that, at the risk of publishing another book very much like many already in print, it is worth while to try it. We have read Dr. Capp's book through, and can truly say that very little fault can be found with it. It is a vast mass of axiomatic truth therein carefully collected and always worth remembering.

E. W. W.

Correspondence.

BERLIN.

(From our Special Correspondent.)

The season of medical congresses opens with the spring. This year, however, spring is found only in the calendar, for the weather is so cold and wet that it resembles November more than April, and consequently diseases usually regarded as due to cold are very prevalent. The causation of these affections was much discussed at the two congresses which have just closed. The Deutsche Gesellschaft für Chirurgie met at Berlin and the Congress für Innere Medicin at Wiesbaden. At both the discussion of Koch's treatment occupied a large part of the proceedings. Professor von Bergmann opened the surgical congress with a paper on tuberculin. At the close he compared Koch's discovery with the old story of the dying

father, who, on being asked by his sons where they would find a treasure he was supposed to have hidden, told them to dig in the orchard. On doing so they found nothing, but the fruit that year was larger and sweeter and more plentiful than ever before, and then they knew what the treasure was. So work and renewed impetus to investigation will be the most valuable result of this discovery. Professor König, of Göttingen, believes it would be very unfortunate if the remedy should be no longer employed, since he has seen cases improve under it more than under any other therapeutic measure. Further, he does not believe that necrosis occurs at the point of action of the solution unless an open ulcer be present, by means of which infection can enter the body from without. Dr. Schede, of Hamburg, regards tuberculin as a very useful weapon in the warfare against disease, and thinks that the varying success in its use depends upon the varying method of its application. Injections, he says, must always be combined with surgical measures, and the initial dose must always be small. It is especially important to remember that there is a possible danger of setting the bacilli free in the circulation, and therefore care must be taken not to reduce the body's power of resistance by causing too great constitutional reaction. The dose may be gradually increased. The interval between the injections must not be too long, since the power of resistance to the remedy established by its use is soon lost. Launstein, of Hamburg, reported results in a number of cases. Von Eiselberg, of Vienna, reported a case of actinomycosis from Billroth's clinic cured by the remedy. Kuster, of Marburg, reports local and general reaction in cases of osteomyelitis, lupus erythematodes, and lipoma.

Senger has experimented with injections of formic acid and iodoform in tuberculous joint-affections with apparently very good results.

It would require too much space to give a complete review of the proceedings of the Congress, and we will confine ourselves to a few interesting and important papers.

Dr. Bender, of Berlin, showed a soldier in whom, after a fall from a horse, epileptic convulsions developed. There had been a wound in the parietal region, which healed of itself. Several months later convulsions appeared. They always began with tremor of the right foot, thigh, and arm, and finally involved the left side also. The skull was trephined, and a portion of brain matter, which, however, showed nothing abnormal, was removed from the motor centre. The convulsions have not returned. Slight weakness of the right forearm and numbness, especially on the ulnar side of the ring-finger, and slight weariness after mental work remain. Professor Gurlt made a report on the use of chloroform. There were 66 reporters and 24,625 administrations of chloroform or ether, as follows :

	Asphyxia.	Deaths.
22,656 pure chloroform	71	6
470 pure ether	0	0
1,055 ether and chloroform	5	0
417 ether and chloroform and alcohol	4	0
27 bromethyl	0	0
	80	6

In 3776 administrations of chloroform, 1 death occurred; in 319 administrations of chloroform, 1 asphyxia occurred; in 211 administrations of chloroform and ether, 1 asphyxia occurred; in 104 administrations of chloroform, ether, and alcohol, 1 asphyxia occurred. In 2732 cases narcosis lasted one hour, and in 278 cases a longer time,—once, 150 minutes; once, 155 minutes; and once, 180 minutes. The greatest quantity of chloroform used was 180 c.c. A few authors always use morphine injections at the time of inhalation, others often, and a few never. Five observers use it often, or almost always, in patients over 15 years; 14 observers used morphine 2194 times out of 6806 inhalations. There was 1 case of asphyxia for every 307 inhalations, whether with pure chloroform or mixed. Tracheotomy was performed successfully in 4 cases; 6 deaths were due to chloroform, and 3 to other causes.

Herr Brun, of Tübingen, reported a case of cystic goitre, in which the growth was so large as to reach nearly to the umbilicus. Operation was successful.

Operative treatment in prostatic disease was exhaustively discussed, and great stress laid upon the necessity of knowing the condition of the bladder, as otherwise urinary trouble may follow. Operations on the gall-bladder were also reported.

Julius Wolf exhibited a girl of 6 years, showing congenital anomalies of most of the joints. She could voluntarily luxate the right knee. There was congenital luxation of the hip-joints and of the radii.

Retin, of Frankfort-on-the-Main, diagnosticated and successfully removed an extradural tumor in the region of the cauda

equina. On examination it proved to be a cavernous lymphangioma.

Besides the above, many interesting papers on surgical bacteriology were read. Among others, Jordan, of Heidelberg, on the etiology of erysipelas; Von Brunner, on the excretion of pathological micrococci by the sweat; Reichel, on immunity from pus bacteria.

On April 4 the corner-stone of the Langenbeck House was laid.

PROFESSOR SEMMOLA'S CRITICISMS OF KOCH'S METHOD OF TREATING TUBERCULOSIS.

To the Editor of the THERAPEUTIC GAZETTE:

DEAR SIR:—In the March number of the THERAPEUTIC GAZETTE appears a translation of Professor Semmola's article from the *Internationale Klinische Rundschau*, purporting to be "A Critical Study of Koch's Cure for Tuberculosis."

The writer of that paper, upon much theoretical reasoning, without any personal observations and without recognizing any of the clinical results obtained, concludes that it is simply impossible for tuberculosis to be cured by Professor Koch's lymph, but expresses his willingness to take back all he has said when he sees the first case of a real cure from the employment of the remedy.

The question even then would arise as to what is a real cure of tuberculosis, and for how long a time must the apparent cure have lasted to make it real? If time is at all required after the disappearance of symptoms, and if, as I should believe, such time should be at least six or twelve months, then his adverse conclusions are entirely premature; for he wrote only three months after the first employment of the remedy, when not even an apparent cure should have been expected from the first trials of any remedy were it ever so valuable or specific, for he himself claims that in our previous experience many months or years had to elapse in climatic and other treatment to accomplish this, and even then experience has shown that the cure may be only apparent, and relapse follow thereafter.

I consider that a real cure of any disease is accomplished when the symptoms have disappeared and the patient has returned to a condition of previous health, but that evidences of the previous disease may remain in the parts or organs having been the seat of structural changes, the cure being nevertheless real.

In tuberculosis, especially of internal organs, it is, however, difficult to say that every tubercle nodule or bacillus has undergone expulsion, or such changes that further pathological processes will not recur, and we have, therefore, not been willing to consider such a case permanently cured until time shall have shown such permanency. If it prove permanent, *the permanency was already established at the time when the cure was only apparent*, and when the last symptom and sign had disappeared.

It is, therefore, not necessary at the present time to show permanent or real cures, we have not had time for the proof of permanency.

In estimating the value of a remedy in a disease which the writer says takes years to apparently cure, even an undoubted improvement, distinctly referable to the remedy in so short a time as three months, should be received gratefully by both profession and patients. If this writer, a year hence, is willing to take back all he has said in adverse criticism, based upon *a priori* reasoning, or at a time when he can be convinced of a permanent or real cure of a single case, it seems strange that he *cannot* at the present time withhold adverse criticism, when, in the very nature of things, time for permanency has not arrived: and when a great number of not only real improvements, but also of apparent cures are already accomplished, which stand in as good a relation of cause and effect to the remedy of Koch as do any other of our therapeutic resources to the diseases for which we have hitherto employed them.

Such criticism is more unjust, misleading, and unscientific, as are heralded reports of cures of cases, perhaps only apparently cured, or possibly only materially improved, and I protest against insinuations made against the judgment of the very foremost of our clinicians all over the world, who do say that they have seen improvement and apparent cures from the employment of this agent. Further, I should be more generously inclined towards the latter, should they all have failed to observe correctly (for the burning desire to get real help in our battle with a hitherto almost unconquerable foe would have been father to the thought), than I would towards the critic, who, without weighing the evidence presented, and prematurely, without having used it, decries a valuable remedy, and by so doing produces suspicion and fear in the minds of those who have had no personal experience.

At the present no one should pass judgment

on Koch's method. Every one of the profession who at all ventures upon its use must do so with the knowledge that it is not an indifferent agent, and may produce the gravest consequences as well as the most happy results.

How to avoid its dangers must be our task for some time to come, and I have already pointed out one source, which I believe to have been overdosage, or too rapid increase in dosage, especially in pulmonary cases. Under a much more conservative use, I have, after three months, no regret to record of its employment in any case, and even in advanced cases I have been able to use the remedy apparently with the happiest results. We have at this writing six cases in which an undoubted arrestment of both subjective and objective symptoms of the local processes is manifest, and which may now be claimed as apparently cured, the general health having also been restored. In two early cases of laryngeal tuberculosis nothing subjective or objective is discernible that would even justify a suspicion of disease.

Even in advanced disease we have ten cases of remarkable improvement of both subjective and objective symptoms, with gain in flesh up to seventeen pounds in two months; and there is now not a single case on this method of treatment in my institution where there is no change for the better. Certainly, if all this improvement is incidental, it must be conceded that the remedy has not retarded it, and I have injected as high as fifty milligrammes, one milligramme of which our critic says is dangerously poisonous.

Even my latest case admitted to this treatment for a sufficient length of time to expect any results should convince our critic that his position is unwarrantable by clinical facts, and I report it here at length as the least of the benefits conferred by this remedy in my hands, but highly satisfactory considering the nature and extent of the affection, and the short time the treatment has been employed.

Mr. P. has suffered from his pulmonary affection for five years, and has lived in this climate on account thereof during this time. His decline has been very gradual, and he has consulted me several times during the last six months, when the physical symptoms present were each time carefully recorded. A record in October last, another on the 29th of December, and again another, February 28, showed the following condition without any material change from one time to the next. A dry cavity in right upper lobe to third rib in front and middle of scapula posterior, dense infiltration to fifth rib in front, and less marked in lower lobe anteriorly, posterior, and lateral. In all the right half of the chest numerous moist râles mask every respiratory sound, both in inspiration and expiration. On the left side there is a cavity, anterior to second rib, with gurgling; infiltration exists anterior and posterior to a level of nipple and lower angle of scapula, respectively, with the same condition of moist râles as noted on right side. Sputum contained tubercle bacilli. On the 29th of December I refused this patient for Koch's method of treatment, but owing to some good results in other advanced cases, I consented to a trial, February 28, and he received his first injection of one half milligramme on March 2. Since that time an injection every third day, the last one of .0015; in all not more than .01 of the lymph has been used, and yet after the second injection of .0005 the patient himself was sensible of its effects by increased cough and expectoration and various other sensations, while unmistakable changes in the lung occurred since, which to-day enable me to show absence of all râles in both lungs, and disappearance of gurgling in the cavity on the left side, and which is now entirely dry. Only upon a very quick and deep inspiration can I hear at its end a few small moist râles anterior in the right side immediately below the cavity. The respiratory sounds are now distinctly audible and distinguishable in their character.

In the mean while his appetite has improved, he has made a slight gain in weight, is less short of breath, the expectoration is greatly diminished, as is also the cough, and he sleeps on that account uninterruptedly all night. The bacilli seem also less in his sputum, which is more mucous and less purulent in character. His life and external conditions have in no wise been changed beyond his change from his own comfortable and commodious residence to my institution.

Is this now all chance and accident? Why has not this occurred before under most painstaking care and management, and under the continuous influence of the same favorable climate?

This terrible poison of which our critic would warn us of has certainly done no harm, and under its use, of which the patient experienced sensible but no distressing effects, a train of symptoms has subsided which we

have endeavored to improve for six months past without having, in any way, been successful.

But, apart from this case, I now have a number of apparent cures, and a large number of radical improvements, which, to me and also to the particular patients, are very acceptable indeed, and which I should have welcomed as readily and gladly had they followed any other method of treatment, or to medication with inorganic substances. Our critic knows as little of their prospective relapses as I know of their permanency. Only I believe that I have common sense and reason on my side, when I accept them for what they are, with the hope and confidence that the remedy which has aided me in bringing them about, will also aid me in preventing relapses in the future, and making the cases of improvement as permanent as possible.

I know very well that many cases may even fall short of apparent cures or much improvement. First, because of their particular constitution and recuperative powers and advanced stage, that will be impossible, but also because the remedy will have been used with less care and discrimination, and without the additional aids which we fortunately possess in climate and general control of our patients. How far the latter may have contributed in our results we, of course, cannot say.

In the mean while we can only thank Professor Koch for what he has given us as an additional means to overcome a disease which, in its fatalities, outnumbers any other known; and we can be thankful even if the great expectations that have attended its advent have not been and never will be realized.

It has in my hands done all that Professor Koch has claimed or suggested it may accomplish; yes, even more; and while honest criticism should ever be welcome in preserving us from error, unwarrantable denunciations are more injurious to the cause than the pardonable enthusiasm which led some to expect too much.

Respectfully yours,

KARL VON RUCK, M.D.

WINYAH SANITARIUM,
ASHEVILLE, N. C., March 20, 1891.

AT IT AGAIN!

To the Editor of the THERAPEUTIC GAZETTE:

DEAR SIR:—I have recently received a copy of a pamphlet issued some time ago by Miss Frances Power Cobbe and Mr. Benjamin Bryan. It is entitled "Vivisection in America," and is in many ways an astonishing publication. I shall at present comment only on the part of it which refers to some experiments made by Dr. Hartwell and myself in the year 1879.

The good faith of Miss Cobbe I do not doubt, though I cannot but realize that zeal without knowledge is a dangerous thing even in so clever a woman. As regards Mr. Bryan the case is different. It became my duty some years ago to publicly convict him of deliberate falsehood. I find it my duty to once more undertake the same unpleasant task.

Mr. Benjamin Bryan has been frequently informed that when the chest cavity of a mammal is opened artificial respiration is necessary in order that life be maintained. A mammal with opened chest cannot breathe for itself, curare or no curare. A first-year medical student could tell Mr. Bryan that fact, and it is impossible to believe that Mr. Bryan is not well acquainted with it. Nevertheless, he continues to assert that whenever artificial respiration has been used in an experiment the animal must have been curarized; and he is rash enough to make this assertion in regard to the animals on which Dr. Hartwell and I worked.

The research to which he refers was one necessitating the natural action of the nerves of breathing on the muscles of breathing. Those nerves thrown out of action, the experiment would have been impossible, and any employment of curare (which paralyzes the motor nerves) was quite out of the question. Moreover, any writhings of an animal suffering pain would have made the research impossible.

But what does Mr. Secretary Bryan assert?

"This [referring to the statement that artificial respiration was used] implies the administration of curare, which would render the ether useless and needless for keeping the animal quiet for a short time."

Truly, he earns his wages! But would he not be wise to share them with a person who has some knowledge of physiology, if perchance he could find such a one willing to bargain with him. An arrangement of that kind

> "Wad fra monie a blunder free him,
> And foolish notion."

H. NEWELL MARTIN.

JOHNS HOPKINS UNIVERSITY, BALTIMORE, MD.

ARISTOL—A PATENT MEDICINE.

To the Editor of the THERAPEUTIC GAZETTE:

DEAR SIR:—The wide distribution of a printed circular by Messrs. Schieffelin & Co., of New York, and Mr. E. N. Dickerson, in which attention is called to the fact that any one in this country will be prosecuted who sells or uses "aristol" not purchased from Messrs. Schieffelin & Co., or who manufacture this compound of thymol and iodine by any process whatever, is a sad commentary on our patent laws which render such doings possible.

Within the last year or two, chiefly through the investigations of Professor Ranke, ("Ueber die antiseptische Wirksamkeit des Thymols-Gasverbands, nach Versuchen in der Gröninger Klinik"), thymol has been proved to be superior to phenol as an antiseptic (see also Nothnagel and Rossbach, Arzneimittellehre).

Aristol is a compound of thymol with iodine, and has been lately brought to the attention of medical men. Patents have been granted by the United States Patent-Office for the control, manufacture, and sale of the article under that name.

No one familiar with the patent laws will wonder at the action of the patent office in granting one more application of this nature.

Chemists, however, are beginning to wonder if all the information embodied in text-books will not be the basis of a series of patents in the near future, providing that the matter be designated by new and euphonious names.

False sentiment for industrial enterprise is out of place. The majority of medicinal patents have no real merit. Most of them represent absolutely nothing that was previously unknown to science; they are nuisances; they do not contribute to the general intellectual progress; they discourage scientific investigations, instead of promoting its stimulating and life-giving properties.

For example, would it not be a crying injustice if chemists, by law, should be prevented from making chloroform or iodoform, substances known over fifty years, according to methods that are laid down in text-books of chemistry, merely because some one had his attention attracted by what people call a formula, and applied for and obtained a patent on a variation of a method of making those articles?

The only explanation that can be given of this lamentable state of affairs lies in the laxity and ambiguity of the present patent laws, and the almost puerile knowledge which they manifest regarding history of chemistry in its broadest sense. A medicinal preparation need not represent anything novel further than the new name; no scientific principle or discovery need be involved. They are patented only for the money that may be made out of them as common ventures; no benefit to science or humanity is intended. Those patentees are good judges of human character!

The genius of the chemical profession as laid down in Poggendorff's and Liebig's "Annalen der Chemie und Pharmacie," offers valuable "germs" for inventions, discoveries, and "patents."

If I am not entirely misinformed, it was known to the medical world that aniline compounds lowered the temperature of the body. Now we are annoyed with a patented preparation of an aniline compound (acetanilide, antifebrin).

Pyoktanin is only a fancy name for a well-known aniline color, the clearly-defined properties of which every microscopist was well aware.

Saccharin was an original discovery. So was artificial indigo, and was artificial vanillin. The promoters of such progress deserve encouragement, and should enjoy financial benefit from their inventions.

But, as stated, thymol was known before aristol was patented.

Aristol is merely an assumed name for dithymoldiiodine, and it is theoretically prepared by adding a thymol solution to an iodine solution (Schmidt, "Lehrb. d. Pharm. Chemie, 1889–90, p. 1502). Aristol, ignoring the deceitful expression of its advocates, the "preparation involves the greatest care and experience;" 1° must give the iodine reactions (a part of it heated in a test-tube will, if genuine, give off the characteristic violet vapors of iodine). This is, however, no warrant that it is a pure article, as it may contain free iodine; 2° must give thymol reactions (dissolve a mere trace in a few c.c. glacial acet. acid; add a few drops of concentrated sulphuric acid and one drop nitric acid.) A beautiful dichroistic fluid is obtained, red by transmitted, dark green by reflected, light, if thymol is present.

Impurities in aristol would be all the by-products, derived from unskilful treatment; it might contain potassium or sodium iodide; free iodine, as stated; it might be adulterated even, for, as a patented article, it is above control.

I would sooner prefer the application of a pure solution of a well-defined, legitimate chemical compound than one upon which no control can be exercised.

But let us look at it under another light. We have a great many much more difficult names to remember than thymol-iodine would be,—mercury iodide, mercurous chloride, sod. hypophosphite, etc. And, as we have intimated above, thymol-iodine is a definite chemical body, capable of control as to purity when brought on the market. Thymol costs at present four dollars a pound; for aristol is charged two dollars an ounce. It is a matter of record that impurities have been found in the aristol now being sold by the patentee.

Why could not the physician call our pharmaceutical preparations by their legitimate names if he wants thymol iodine? If he wants to try the use of it instead of iodoform, why not say so, rather than pander to the debasing tendency towards quackery by indorsing "aristol" upon his prescriptions, of which he knows nothing?

It is the *laisser aller* system that is at the bottom of all these patent or patented medicines. We, analysts, must get acquainted with microscopical research and physiological experiments. Poisoning cases may call for spectroscopical investigations even, at any time; this is not the place to dwell upon this subject. If the physician would take a little trouble and get a better insight into the chemical identity of the new articles he wants to prescribe, the ethics of medicine and pharmacy would be largely benefited.

J. B. NAGELVOORT, PH.G.

DETROIT, April 27, 1891.

NEW YORK, 16th April, 1891.

ROBERT MEADE SMITH, ESQ.,
EDITOR THERAPEUTIC GAZETTE,
322 SOUTH TWENTY-FIRST STREET,
PHILADELPHIA, PA.:

SIR:—I desire to call your attention to letters patent of the United States granted to Josef Messinger & Georg Vortmann (assignors to Edward N. Dickerson), February 24, 1891, No. 446,875, for the substance now commercially known as "aristol," which is a compound of iodine and thymol.

Messrs. Wm. H. Schieffelin & Co. are the exclusive agents for this product in the United States, and I warn all parties against dealing in that substance unless purchased from them.

It is also illegal and an infringement of said patent to manufacture said substance in any way whatever in the United States.

I am the owner of the patent, and will promptly prosecute all infringements brought to my attention.

I desire, likewise, especially to call your attention, as editor of the THERAPEUTIC GAZETTE, to an article published by you on *October 15, 1890*, at page 18 of your GAZETTE, in which you describe a method of making aristol. As above stated, I own the patent for this combination, and trust, therefore, that you will refrain from using your influence in leading practitioners to infringe this patent to their own detriment.

I shall be obliged to you for inserting a statement of the facts in your GAZETTE.

Yours truly,

E. N. DICKERSON.

[Things have come to a pretty pass when hitherto reputable drug-houses not only take up the manufacturing of proprietary medicines, but even attempt to suppress information as to their nature. It is the existence of this mercenary spirit in the drug trade, which inspired the above letter, that keeps the druggist on a par with other shop keepers with whom money-making is the only thought. It is high time that the medical profession should take some action in this matter: its nature and direction are self-evident, for a manufacturing druggist who thus acknowledges money-making as his only principle may be expected to live up to this principle in the manufacture of his pharmaceutical preparations so as to leave the widest margin of profit.

Fortunately, the virtues of aristol and its alleged advantages over iodoform, chrysarobin, etc., are not so pronounced as to cause any hesitation in relegating it to the class of patent medicines, where its mode of introduction and manipulation by Messrs. Schieffelin & Co. entitle it to a place.—ED.]

Notes and Queries.

CONGRESS OF AMERICAN PHYSICIANS AND SURGEONS.

The meetings of the Congress of American Physicians and Surgeons will be held in Washington, from 3 to 6 P.M., September 22, 23, 24, and 25, 1891.

WILLIAM PEPPER,
Chairman of the Executive Committee.

PARKIN PRIZE ESSAY BEQUEST.

In the terms of the bequest made to the Royal College of Physicians of Edinburgh by the late DR. JOHN PARKIN, Fellow of the College, a prize is hereby offered for the best essay "On the Curative Effects of Carbonic Acid Gas or other Forms of Carbon in Cholera, the Different Forms of Fever, and other Diseases."

The prize is of the value of one hundred pounds sterling, and is open to competitors of all nations.

Essays intended for competition, which must be written in the English language, to be received by the secretary not later than 31st December, 1892. Each essay must bear a motto, and be accompanied by a sealed envelope, bearing the same motto outside and the author's name inside.

The successful candidate must publish his essay at his own expense, and present a printed copy of it to the college within the space of three months after the adjudication of the prize.

In name and by authority of the council of the college.

G. A. GIBSON, M.D.,
Secretary.

9th March, 1891.

THE INFLUENCE OF EXERCISE ON DIGESTION.

DR. STRENG, in a lecture before the Medical Society of Giessen on the "Influence of Exercise on Digestion," which has been published in the *Deutsche Medicinische Wochenschrift*, states that he concludes from his own experiments that this influence is of a retarding nature. His experiments, however, suffer from the fact that he always injected three hundred cubic centimetres of water before obtaining the contents of the stomach, so that the proportion between gastric juice and water continually varied. The first experiments in the clinic at Giessen were made on two dogs. Twenty-five grammes of meat, suspended in three hundred cubic centimetres of warm water, were twice injected into the fasting stomach, and after one feeding the dogs were compelled to remain for three hours in absolute bodily rest, while after the other feeding they were made to take active exercise. After the three hours the contents of the stomach were obtained and analyzed. The quantity did not essentially differ in the two cases; the experiments consequently tended to prove that exercise does not influence the time required for digestion. The chemical analysis also detected no difference. The same results were obtained by substituting the white of an egg for the meat. The experiments were then repeated twenty-five times on three men with healthy stomachs. Two of these suffered from sycosis, and the third from incipient muscular atrophy. They were fed each time with two hundred grammes of minced meat, a bun, a plate of bouillon, and three spoonfuls of mashed potatoes, and the contents of their stomachs were obtained four hours and a half afterwards. The exercise after meals consisted partly in gymnastics, partly in walking; absolute rest was obtained in bed. These experiments gave the same results as those on the dogs, the difference resulting from the chemical analysis being especially imperceptible. The author, therefore, concludes that the gastric function is in no way influenced either by muscular action or by absolute rest.—*Lancet*, March 7, 1891.

REDDENING OF CARBOLIC ACID.

The cause of the intense red coloration frequently observable in carbolic acid after storage for a short period has been the subject of much patient investigation in continental pharmaceutical circles during the last decade. The ill-success that has attended many of these researches is no doubt due to the small quantity of impurity or impurities necessary for the production of a visible effect, so that the absolute conditions under which reddening occurs have been recognized by a few observers only, and the nature of the chemical changes involved is still a matter of uncertainty. The first general impression that the reddening of carbolic acid is a sign of insufficient purity has been removed by the observation that this property is also possessed by synthetic phenol, concerning which there can be no question of contamination with tarry products. Moreover, it has not been shown that the reddened phenol has deteriorated in medicinal value; but the preference for a colorless preparation is only natural, and is expressed as a demand in the new German Pharmacopœia. Hager first stated that a red coloration can be produced in carbolic acid by ammonium nitrite, and later Finzelberg, Meyenbeck, Fabini, and

others attributed the same effect to the action of several heavy metals, notably that of copper. These latter observations are in accord with the fact that pure carbolic acid shows less tendency to redden when not stored in metallic cases. E. FABINI, in a series of articles in the *Pharmaceutische Post* (January, pp. 1, 25, 41, 61), now claims to have isolated the red coloring-matter in an approximately pure state, and to have determined the exact conditions of its formation. He further indicates the probable courses of the reactions involved in the synthesis of the dye, but this suggestion must be substituted by further data before it can be seriously considered. By further study of the action of copper on carbolic acid, Fabini found that the coloring material was formed most rapidly by digestion of cupric sulphate, instead of the metal, with the ammonium salt of carbolic acid. Prepared by this method and extracted with ether the dye proved to be a black, odorless, and tasteless resinoid body, that sublimes upon heating, gives a characteristic blue coloration with concentrated sulphuric acid, and yields a residue in which no trace of copper can be detected. It dissolves in alcohol with a red-brown, in ether with yellow, and in chloroform with yellowish-red color, and even in the proportion of 1 to 300,000 produces a beautiful red color in carbolic acid. He suggests that copper enters the phenol molecule with simultaneous elimination of water, according to the equation $Cu + 2C_6H_5.OH = (C_6H_5)_2.CuO + H_2O$, and that the phenyl copper oxide so formed is reduced by further phenol molecules to copper and an oxidation product of carbolic acid, which he does not pretend to identify. The process repeats itself, and is thus one of continual oxidation. In support of this theory, he states that, though a trace of copper will produce a large quantity of dye, carbolic acid, completely freed from all traces of metals, does not redden, nor is the coloration produced so long as an oxidation agent, like hydrogen peroxide, is present. The presence of ammonia, or rather the ammonium salt of phenol, appears to be also necessary to the formation of the dye, and some connection apparently exists between the ready absorption of ammonia from the atmosphere by carbolic acid, the liquid nature of the ammonium salt and the occurrence of the red coloration in the liquefied portion of the carbolic acid. If copper and ammonia be present in the carbolic acid, the access of air does not appear to affect the result, since, according to Fabini, the phenol can supply by its own oxygen for the oxidation process. The remedy appears to be the total prevention of contact with metals during the process of manufacture and storage.—*Pharmaceutical Journal and Transactions*, February 28, 1891.

A NEW HYPNOTIC MIXTURE.

In the *Journal de Médecine de Paris* for March 22, 1891, DR. STEFANI calls attention to a new hypnotic, which, even if it be not very efficacious, at any rate has the merit of being perfectly harmless. This mixture consists of equal parts of tartaric acid and sodium bicarbonate, the sodium bicarbonate being dissolved in water, the tartaric acid then added, and the mixture drunk while effervescing, from ½ to 2 drachms being given at bedtime. It does not seem probable that, strictly speaking, this mixture, which differs from a Seidlitz powder only in the relative properties of the ingredients, can have any hypnotic power whatever, although perhaps, as Stefani claims, carbonic acid may be endowed with some slight hypnotic power.

CREOSOTE IN DIABETES MELLITUS.

According to VALENTINI (*Les Nouveaux Remèdes*, March 8, 1891) creosote administered internally may be of considerable service in the treatment of diabetes mellitus. The author reports two cases, in which at first 4 drops of creosote were given daily, and the quantity then gradually increased to ten drops in twenty-four hours. Under the influence of his remedy it is claimed that the sugar disappeared, and did not return even after the patients had again commenced to use starchy food.

UROBILINURIA CAUSED BY TUBERCULIN.

DR. G. CAVALLERO reports (*Gazetta Medica di Torino*, February 5, 1891) the occurrence of urobilinuria in three cases treated by Koch's method in the clinic of Professor Forlanini at Turin. Urobilin, with traces of albumen in two of the cases, was found in the urine during the fever of reaction; in one of them these substances appeared at the time when reaction was due after an injection, though no other reactive phenomena were observed. Urobilinuria persisted, though only to a very slight extent, on the day following the injection. Cavallero thinks the excretion of uro-

bilin is an effect of an alteration of the liver, similar to that observed by Hayem in the course of acute infective diseases, and by him attributed to the passage through that organ of toxic substances circulating in the blood during such disorders. The hæmoglobin in the blood is transformed into urobilin, as happens in malarial infection, according to Mya. Tuberculin, therefore, acts like an acute infective fever, producing changes in the liver (degeneration of the hepatic cells?) and in the red corpuscles.—*British Medical Journal*, March 7, 1891.

CHICAGO PASTEUR INSTITUTE.

According to the second report of the Chicago Pasteur Institute for the Preventive Treatment of Hydrophobia since the opening of the Chicago Pasteur Institute (July 2, 1890), 55 persons have received treatment.

31 came from Illinois, 10 from Iowa, 4 from Indiana, 2 from Ohio, 2 from Minnesota, 1 from Missouri, 1 from Tennessee, 2 from Kentucky, 1 from South Dakota, 1 from Arizona.

36 were male and 19 female.

The youngest patient was 2½ years old and the oldest 56. 51 were bitten by dogs, 3 by cats, and 1 by a skunk.

31 persons were bitten in the hands and arms, 3 in the face, and 20 in the body and legs. 24 had their wounds cauterized with chemical agents, and 31 had not.

33 persons were bitten by animals recognized and ascertained of being rabid, by experiments made upon rabbits, by the death of persons and other animals bitten by the same, or by symptoms shown during life, and 22 persons were bitten by animals strongly suspected of being rabid.

All the persons treated are now enjoying good health.

Adhering to the principles of strict and careful sterilization of all instruments and fluids used, no abscesses nor inflammations, nor even irritation of any kind, occurred at the seat of inoculations, thus testing the *purity* of the material used.

It has been made a practice at this institute never to submit persons to treatment *unless in need of it.* Consequently 96 persons were refused treatment, as not reasonable evidence was produced to demonstrate the madness of the animals. All these persons are also in good health, confirming the correctness of our judgment.

EXPERIMENTS TO DETERMINE THE CENTRE OF RESPIRATION.

Dr. Laborde communicates to the *Comptes-Rendus de la Société de Biologie* the results of experiments made by him to ascertain the nerve-centre for respiration, promising a larger work at some future time. He found that superficial mechanical injury to the region of the alæ cinereæ does not accelerate respiration; a deep puncture decreases, or even temporarily arrests, respiration; if the injury penetrates at least to the middle of the substance, respiration may cease altogether. This result is always obtained if a certain circumscribed portion of the substance is cauterized with the hot iron. This portion need in the rabbit be only half a millimetre in diameter, in the dog from one to two millimetres. The iron must, however, enter immediately above the apex calami, and must penetrate at least half the substance from the raphe. If the injury is unilateral, respiration may continue for some little time on the opposite side. Total separation of the medulla below the apex calami always arrests respiration of the trunk, while that of the head continues for some time. Spinal reflexes continue, and even increase; irregular superficial contractions of the respiratory muscles, leading to no results, may be observed. The increase of the reflex action is especially remarkable in new-born animals. No parts of the brain above the medulla oblongata, including the cortex, the corpora quadrigemina, and thalami optici, have any specific influence whatever on the respiratory muscles.—*Lancet*, March 7, 1891.

INFLUENCE OF COLORING-MATTER OF WINE ON DIGESTION.

Dr. Hugounenq has made a number of experiments with artificial digestive fluids, which have led him to formulate the following conclusions (*Répertoire de Pharmacie*, April 10, 1891):

1. All wines without exception interfere with the action of pepsin. Those which are most highly charged with coloring-matter, with alcohol and cream of tartar, are the most hurtful.

2. The acidity of new wines is incapable of aiding the action of pepsin.

3. Among the coloring-matters artificially and fraudulently introduced into wines, methylin blue, azoflavine, and, above all, fuchsine interfere with peptic digestion; while the vegetable coloring-matters, such as black

mallow, elder, and œnoline also exercise unfavorable action.

4. In removing a part of the cream of tartar plaster removes from wine an element which tends to slow the action of pepsin. Digestion is more rapid, therefore, with plastered wines than with natural wines.

ESSENCE OF CINNAMON IN MALARIA.

Dr. Capsus states in *La Pratique Médicale* for April 7, 1891, that in the hospital in Marguelane, in Turkistan, excellent results have been obtained in the treatment of all forms of malaria by sprays of the essence of cinnamon. Even cases which have resisted the action of quinine and arsenic improved in a few days under this treatment. The spraying is performed several times daily in the hospital wards, and is stated to be much more efficacious than a similar procedure with the essence of eucalyptus.

DANGERS OF SULPHONAL.

Although sulphonal is probably one of the safest, as it is one of the most efficacious, among the hypnotics recently introduced, the series of cases published by Bresslauer, of Vienna, show clearly that it has certain dangers. The degree of peril is difficult to estimate, as the patients were lunatics, and were also apparently feeble; but the fact is significant that out of seventy-seven patients who were treated with the drug, no less than seven showed serious symptoms, and in five of these there was a fatal termination. It ought to be mentioned that the patients had been taking the drug for a considerable time in good doses, and had borne it well until symptoms of disturbance set in, these being great constipation, dark-brown urine, slow, or in some cases rapid but feeble pulse, discolored patches resembling purpura on the limbs, and great prostration. In the cases which ended fatally, the cause of death was heart-failure, with œdema of the lungs.—*Lancet*, April 4, 1891.

CHLORAL AS A COAGULANT.

Though hydrate of chloral is generally used in medicine, it is not without its advantages in surgery. According to Dr. Marc Sée it possesses the property of coagulating blood and serous fluids, and may be made to replace the iodine solution generally injected into hydroceles. He himself has treated two hundred hydroceles with chloral without the occurrence of any accident. He employs for this purpose a ten per cent. solution, an ounce of which is injected all at once, or very slowly, into the sac. Two or three days afterwards a large effusion of fluid into the tunica takes place, but is soon entirely reabsorbed. Where the hydrocele wall is much thickened, injections of chloral, or, indeed, of any kind, are useless, and recourse must be had to free incision. The chloral solution above referred to may be repeatedly injected, with advantage, into the neighborhood of varicose veins, as it causes the blood gradually to coagulate, and the veins to contract. Some trials have also been made with chloral as an injection into vascular tumors, but hardly sufficient to warrant any definite report.—*Lancet*, February 14, 1891.

THE DANGERS OF CALOMEL IN CONJUNCTIVITIS.

Dr. Piedallu reports, in the *Lyon Médicale* for March 29, 1891, that one of his patients having accidentally introduced some ipecac into the eye, and this being followed by suppuration and a large ulceration of the cornea, he instituted an antiseptic treatment, which was completed by the introduction of a pinch of calomel, with an equal part of powdered milk-sugar. After about fifteen minutes the patient complained of intolerable suffering. There was great swelling of the eyelids, with protrusion of the conjunctiva. On making inquiry, Dr. Piedallu learned that his patient for the last six months had taken from fifteen to thirty grains of potassium iodide daily, and analysis of the tears showed that they contained large quantities of iodine. A violent caustic combination was, therefore, evidently formed between the calomel and the iodine, with the most disastrous effects, for although the eye was not completely destroyed, vision was almost totally lost. This unfortunate accident is well worthy of attention, so that the repetition of such an unfortunate state of affairs might be avoided. Before calomel is introduced into the eye, inquiry should first be made as to whether the patient has been on iodine treatment.

A CORRECTION.

In the article published in the April Gazette, by Drs. Gibbes and Shurley, reference is made on page 221 to an emulsion of "oil of eulicum." This is a typographical error. It should be eulachon oil.

X